PROPERTIES OF TEMPOROMANDIBULAR JOINT NOCICEPTORS IN NORMAL AND INFLAMED TISSUE

BY

BARRY LOUGHNER

A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

1992

I dedicate this work to my daughter, Carina Beth.

ACKNOWLEDGEMENTS

I thank Dr. Brian Cooper, Ph.D., for his technical guidance in the research involved in this dissertation. I thank Ms. Martha Oberdorfer for her technical assistance. I thank Dr. Parker Mahan, D.D.S., Ph.D., and Dr. Arnold S. Bleiweis, Ph.D. for their strategic guidance. I thank Dr. Robert Bates, D.D.S., M.S. for his administrative assistance.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

KEY TO SYMBOLS

- • Vertical plane or previously inflamed tisue.
- Δ Horizontal plane or acutely inflamed tissue.
- \+ Saline control tissue.

Abstract of Dissertation Presented to the Graduate School
of the University of Florida in Partial Fulfillment of the
Requirements for the Degree of Doctor of Philosophy

PROPERTIES OF TEMPOROMANDIBULAR JOINT NOCICEPTORS
IN NORMAL AND INFLAMED TISSUE

By

Barry Loughner

May, 1992

Chairman: Parker Mahan, D.D.S., Ph.D.
Cochairman: Brian Cooper, Ph.D.
Major Department: Oral Biology

Mechanical response properties of nociceptors of the goat temporomandibular joint (TMJ) were characterized by unit recordings from the trigeminal ganglion. Populations of afferents were sampled in normal tissue and in tissue previously inflamed (PI) with carrageenan for at least 6 hours prior to testing. In other experiments, nociceptors were characterized in normal tissue and then retested for up to 3 hrs subsequent to exposure to carrageenan (AI). To produce mandibular movement in the vertical and horizontal planes, dynamic and static forces were applied to the mandibular pole. Stimuli were quantified by force and angular displacement transducers. Receptive fields were small, single spots (2-3 mm) and located on the lateral or posterior capsule of the TMJ. Conduction velocities were shown to be in the group III and IV range. Stimulus-interval data was best described by power functions. Assessment of force-movement relationships indicated that capsular nociceptors responded exclusively to intense forces that produce extreme displacements of the mandible.

In normal tissue, 24 of 36 nociceptors transduced dynamically applied stimuli (mean activation threshold for dynamic force = 15.9 $\pm$ 11.3 N and for force velocity = 17.3 $\pm$ 18.9 N/s). Relatively fewer units transduced static force (8/36) or position (1/36).

In PI conditions, tests revealed enhanced reactivity for dynamically applied stimuli. Mean power functions for dynamic tests in PI conditions (LnISI = -1.3 LnF + 7.3) had steeper slopes compared to those in normal tissue (LnISI = -1.1 LnF + 5.4) and were shifted graphically to regions indicating greater reactivity (below and to the left of those in normal tissue). These shifts were suggestive of sensitization.

In AI conditions, 8 of 11 nociceptors acquired either dynamic or static coding ability. Acquired coding ability also appeared in nociceptors (n = 2) that were without transducing capacity in normal tissue. Acquired reactivity for vertical plane movement was also seen for those nociceptors (n = 3) that were reactive only to movement in the horizontal plane in normal tissue. Acquisition of coding ability following carrageenan-induced inflammation suggested afferent sensitization.

CHAPTER 1

INTRODUCTION

The temporomandibular joint (TMJ) is the site of a number of disorders that burden the health care system and extract a large cost in human suffering (Helkimo, 1979; Solberg, 1987). Afferent groups presumed to mediate TMJ pain are likely to play a role in a variety of TMJ disorders. Many theories have been proposed to explain TMJ pain and dysfunction (Deboever, 1973; Dubner et al., 1978, Yemm, 1979). These theories propose both intra- and extra-articular origins of TMJ pain. Intra-articular theories argue that pressure or tension on articular tissues results in TMJ pain. Extra-articular theories propose that muscles or other contiguous structures refer pain to the TMJ (see Appendix A). Fundamental to an evaluation of intra-articular theories is an understanding of the response properties of TMJ nociceptors.

Our understanding of nociceptors innervating articular tissues has been advanced in recent years (Schaible and Schmidt, 1983a, b, 1988b; Guilbaud et al., 1985; Birrell et al., 1990). Most detailed information concerning the response properties of joint nociceptors has come from studies of the cat knee and rat ankle joint. While there is considerable information regarding the neuroanatomy of the TMJ (see Appendix C), little is known about the physiology of nociceptors of the temporomandibular joint.

Early studies examining properties of afferents innervating the cat knee joint reported activation of slowly conducting, myelinated fibers only by forceful rotational movements beyond the physiological range of motion (Burgess and Clark, 1969; Clark and Burgess, 1975). In contrast, Schaible and Schmidt (1983b) identified populations of

small fibers that were activated by passive movement of the knee joint, both within and beyond the normal range of motion. These afferents were categorized into four populations on the basis of their response range. Afferents of populations I and II responded to innocuous joint movement in the normal range of motion, but population II responded best to forceful rotation. Population III units were activated exclusively by forceful movement and population IV had no response to movement. Based on movement sensitivity, afferents that responded within the normal range of motion were not considered nociceptors, while those that respond beyond the normal range were nociceptors. Subsequent studies by Schaible and Schmidt (1985, 1988b) concentrated on populations III and IV. However, despite the importance of range for classifying afferents, distinctions between normal and non-normal ranges have been ancedotal. Quantification of the relationship between range of motion and afferent activity is still pending.

There are no studies that have examined properties of TMJ nociceptors. Previous reports have examined the discharge characteristics of afferent traffic in the auriculotemporal nerve that may contribute to position sense and control of mandibular movement (Kawamura et al., 1967; Klineberg et al, 1970, 1971; Kawamura and Abe, 1974; Lund and Matthews, 1981). While TMJ nociceptors may have properties similar to those described for cat knee joint, there are considerable functional and anatomical differences between these two joints that indicate that properties of TMJ nociceptors should be determined (see Appendices C and F).

Changes in the properties of TMJ nociceptors (sensitization) may account for some of the symptoms of TMJ dysfunction. These symptoms include pain during mandibular movement, pain on local joint palpation, and tonic pain. Changes in nociceptor properties are likely to be necessary to the development of these forms of pain. As pain on movement is a primary symptom of TMJ dysfunction, a precise determination of the relationship between movement and afferent discharges is valuable. Quantification of force and movement also permits more direct specifications of movements which are outside the

normal range of motion, and identification of afferents that respond specifically in these ranges.

Sensitization of TMJ receptors may be an important defense mechanism that protects the joint from excessive movement which may cause injury. The TMJ is often the site of inflammations associated with various forms of TMJ dysfunction (e.g. arthritis and synovitis). An understanding of how inflammation may modify TMJ afferent function would reveal the form and range of TMJ afferent sensitization and lead to a better understanding of both etiology and treatment.

Sensitization of nociceptors has been documented in the cat knee joint (Coggeshall et al., 1983; Schaible and Schmidt, 1985, 1988b; Grigg et al., 1986) and in the rat ankle joint (Guilbaud et al., 1985) following chemically-induced acute or chronic arthritis. Acute arthritis in the cat knee joint, induced by carrageenan and kaolin, produced changes in the discharge properties in joint afferents. These changes include an increase in the proportion of small fibers that could be activated by innocuous joint movement, recruited units, and the appearance of spontaneous activity. Studies of sensitization of TMJ nociceptors may provide uniquely important information regarding short and long term changes occurring in TMJ afferents following local trauma, arthritis or chronic disc displacement.

In the following experiments, we examined properties of TMJ nociceptors in both normal and inflamed tissue of the goat. The goat is an excellent model for TMJ physiology because of functional and structural similarities to humans including range of motion and innervation of the auriculotemporal nerve. (See Appendices C and F).

CHAPTER 2

METHODS

Subjects

Experiments were performed on 59 goats, ages 6 - 12 months and weighing 30 - 60 lbs. All goats were kept in pens at the veterinary hospital. Goat health was monitored and maintained by animal care technicians, veterinary staff and faculty. All procedures were approved by an internal review board (protocol 7136).

Exposure of the TMJ and Trigeminal Ganglion

Rompun (3 mg/kg) and Ketamine (11 mg/kg) were given as preanesthetics. Anesthesia was induced with a-chloralose (7.5 mg/ml) via a lactated ringers drip. If necessary, pentabarbitol was periodically administered intravenously to maintain deep anesthesia. Goats were artifically respirated at a rate of 10-20 breaths per minute. Blood pressure, body temperature and end-tidal CO_2 were continuously monitored and maintained within physiological limits. At the conclusion of each experiment, the goats were euthanized with saturated KCL.

To expose the right TMJ, the skin was removed from the lateral posterior aspect of the face. The parotid gland, pinna and the zygomaticoauricularis muscles were removed to access the posterior portion of the TMJ capsule. The styloid process and associated muscular and ligamentous attachments were clipped off at the sphenoid bone. The origin of

the sternomastoid and caudal digastric muscles were excised from the mastoid process and jugular process of the occiput, respectively. The sphenomandibular ligament and fatty tissues were removed. Care was taken to preserve the microvasculature of the TMJ capsule. The exposed capsular tissue was kept moist by repeated applications of physiological saline.

Several nerves were cut distal to the trigeminal ganglion in order to avoid recording activity other than TMJ afferents. The buccinator nerve was severed as it passed the anterior border of the masseter muscle. The masseteric nerve was cut as it entered the deep and superficial masseter muscle. The posterior trunk of the mandibular nerve was cut distal to the branching of the auriculotemporal nerve. As a consequence, afferents of the lingual, inferior alveolar and mylohyoid nerves were eliminated.

The trigeminal ganglion was accessed via its position caudal to the foramen ovale. Removal of the thin, lateral plate of bone of the tympanic bulla and the tympanic plate exposed the ossicles of the middle ear and internal surface of the tympanic membrane. Removal of the inferior aspect of the greater wing of the sphenoid and the inferior aspect of the petrous bone exposed the caudal surace of the trigeminal ganglion. Access to the ganglion is improved by removing the sphenomandibular ligament and fatty tissue in the infratemporal fossa.

Recording Procedures

Extracellular recordings were made by penetration of the trigeminal ganglion with tungsten microelectrodes (Microprobe, Inc.) until unit potentials were evoked by passive jaw movement. Most units were found in the posterior region of the trigeminal ganglion. (See Appendix E). Receptive fields were then identified on the lateral or posterior capsule of the TMJ. Amplified output was led to and monitored by a digital oscilloscope and an audio speaker. Data was digitized and stored on video tape (Vetter Instruments, Model No.

3000A). Data were recovered from tape for analysis with an RC computerscope (RC Electronics) or captured on a line by a thermal printer (Astromed, Dash IV).

After a unit was characterized, the conduction velocity was determined by measuring the latency of responses to suprathreshold electrical stimulation applied to the receptive field on the TMJ capsule. Electrical stimulation was performed with a Grass S88 stimulator and isolated, constant current unit. Square-wave pulses of 0.2 to 2 msec duration were applied with monopolar electrodes. Conduction distance was estimated in situ.

Characterization of TMJ Afferents

Once an afferent was isolated, passive jaw movements were used to determine which type of movement was preferred (preferred movements were those which produced the most vigorous response). Jaw movements included: 1) vertical jaw movements from the closed to the open position. Afferent responses to vertical jaw movements were termed "vertical plane reactivity" (VP); 2) lateral jaw movements from the closed to extreme lateral position. Afferent responses to the lateral jaw movements were termed "horizontal plane reactivity" (HP).

A force probe was used to produce jaw movement. The probe consisted of an axial force transducer (Entran Instruments, Model ELF TC500-20) embedded in a plexiglass rod. The transducer monitored forces used to move the jaw in the vertical or horizontal plane. The probe was applied to fixed points of a bit which was mounted to the incisal teeth of the mandible at the midline. Force and jaw movement were recorded on video tape along with afferent activity. Jaw movement was monitored by an angular displacement transducer (ADT, Trans-Tek Model # 604-001) mounted above the right TMJ (Figure 2-1). Using the probe, both dynamic and static forces were applied to the mandible (Figure 2-2).

Figure 2-1. Mandibular movements were produced by a hand held probe. Force applied to the mandible was quantified by a force transducer. Vertical plane mandibular movement was quantified by an angular displacement transducer mounted above the right TMJ and attached to the mandibular pole by a slide assembly. Vertical plane movement of the mandible was produced by applying force at point A on the jaw movement apparatus. Horizontal plane movement was produced by applying force at point B. Afferent recordings were made following exposure and penetration of the trigeminal ganglion proximal to the foramen ovale.

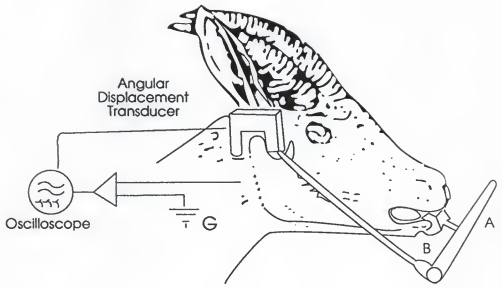
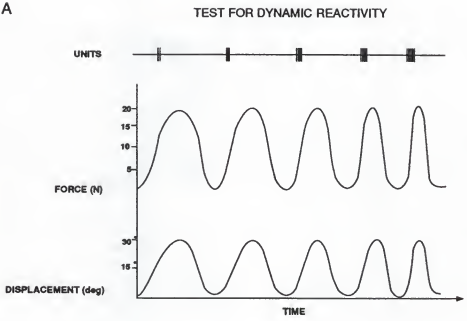
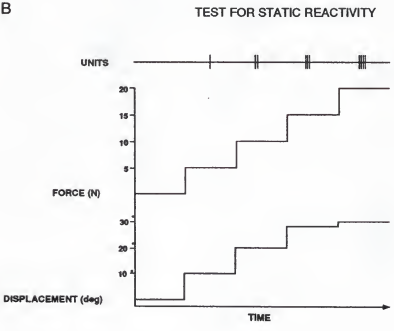

Angular
Displacement
Transducer
Oscilloscope
G
A
B

Figure 2-2. Dynamic and static test series for force, displacement and velocity. A) Dynamic test series. Sawtooth patterns of successively increasing velocities. B) Static test series. Stepwise pattern of successively increasing force and displacement.

A


TEST FOR DYNAMIC REACTIVITY
UNITS
20
15
10
5
FORCE (N)
30
15
DISPLACEMENT (deg)
TIME

B


TEST FOR STATIC REACTIVITY
UNITS
20
15
10
5
FORCE (N)
30
20
10
DISPLACEMENT (deg)
TIME

Isolated units were characterized by two series of jaw manipulations. The first series consisted of five tests of reactivity to dynamic force. The first, at a low velocity, was followed by jaw movements of progressively higher velocities. The range of velocities was approximately 0.3 to 250.0 N/sec. The second series consisted of five stepwise, static force applications. Each step was maintained for approximately 2 seconds. Forces up to 120 N were applied.

To confirm that jaw movement activated afferents of the TMJ capsule, receptive fields on the capsule were identified and characterized for each case. Thresholds for activation of mechanosensitive afferents on the capsule of the TMJ were determined by the bending force of von Frey filaments (monofilament nylon) of different stiffnesses. The method of limits was used to determine threshold. Nylon probes were applied to the capsular field until the minimum force required to activate the afferent was determined. In some cases, no receptive field could be found. This group of cases was treated separately from afferents with identified receptive fields.

Statistics

Nociceptors were defined as those afferents that responded preferentially to extremes of jaw movement. Relationships between force applied and jaw movement were assessed to determine whether the afferents reacted at movement extremes. Force-movement data was plotted for all units ($n = 10$) that responded preferentially to vertical jaw movement and produced significant functions. Momentary relationships between force, jaw movement and unit activity were determined. Force-interspike interval, movement-interspike interval and velocity-interspike interval records were fit to linear, logarithmic, exponential or power functions using simple linear regression (Statistical Analysis System, SAS). The best fits were determined by comparison of coefficients of determination.

For analysis of static reactivity, regression data were "segmented and balanced." A segment (or step) of force was added to the regression model until the coefficient of determination was maximal. The regression was "balanced" by using only six scores for each stepwise force segment. This procedure avoids weighting the regression differentially at higher steps, where more scores typically bias the regression. These procedures were not possible on tests of dynamic force reactivity. Therefore, for dynamic force or movement tests, all spike intervals were used until a minimum interval was obtained.

Several characteristics of regression lines were subjected to analysis. These included force-activation thresholds, movement-activation thresholds, force-frequency asymptotes, movement-frequency asymptotes, mean response intervals, slopes and intercepts. Force-activation thresholds (FAT) and movement-activation thresholds (MAT) were defined as the instantaneous force or degree of movement at the first response interval. Force-frequency asymptotes (FFA) and movement-frequency asymptotes (MFA) were defined as the force or movement at which the frequency response was maximal (i.e., minimum response interval). The FAT or MAT paired with the FFA or FMA were used as the lower and upper boundary values to plot functions derived from regressions. The mean response interval (MRI) was calculated from the regression equation by using the mean force or movement value calculated from the boundary values (FAT + FFA/2 or MAT + MFA/2). Force-frequency thresholds and movement-frequency thresholds (FFTs and MFTs) were determined for each unit that was tested for static reactivity. The FFT and MFT were defined as the minimum force or movement which would maintain a sustained discharge of the afferent. Slopes, intercepts and coefficients of determination were generated only from significant regressions. Unit reactivity that could not be described by significant functions were called "non-coding" or "non-transducing" afferents.

"Sensitization" refers to the enhanced excitability of TMJ afferents that may occur following carrageenan-induced inflammation. Enhanced excitability is reflected quantitatively as changes in response properties of TMJ afferents in normal and in inflamed

tissue. Sensitization was assessed qualitatively by comparisons of functions fit to units in normal and inflamed tissues.

Shifts of stimulus-response coding functions were used as an indication of enhanced reactivity. Significant functions generated from responses of afferents in inflamed tissue that were located graphically below and/or to the left of functions fit in normal tissue were suggestive of sensitization (See Figure 2-3). Significant functions that were acquired in inflamed tissue but not expressed in normal tissue also were considered to represent sensitization. Sensitization was assessed quantitatively by statistical comparisons of function characteristics generated from stimulus tests on units in normal and inflamed conditions. Function characteristics (slope, intercept, thresholds, asymptotic activity, coefficients of determination and mean interval) were compared in normal and inflamed conditions using a one-way ANOVA (Li, 1967) for between subject and t-tests for within subject's comparisons. Only significant functions contributed to the analysis.

Experimental Inflammation

Inflammation of the TMJ was induced by injection of 200 µl of 2% carrageenan (Sigma Chem.). In some cases, units were characterized in normal tissue and then exposed to carrageenan. If the receptive field was located on the lateral side of the capsule, carrageenan was dropped directly onto the receptive field as well as injected into the area of the receptive field. If the receptive field was located on the posterior side of the capsule, carrageenan was injected into the area of the receptive field. The remainder of the carrageenan was injected into the superior joint space. Subsequent testing was performed after at least 30 minutes and continued for up to 3 hours. In other cases, units characterized in normal tissue were treated with saline. The injection of saline and subsequent retests were identical to those used with carrageenan. In other cases, response properties of separate populations of TMJ afferents were examined only in normal or pre-inflamed

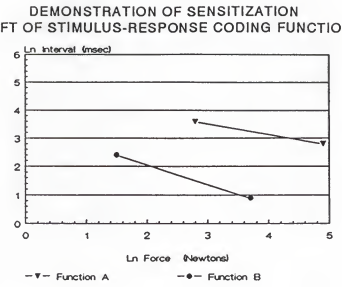


Figure 2-3. Demonstration of sensitization as a shift of stimulus-response functions. Shifts of significant stimulus-response functions to graphic zones of enhanced reactivity (below and to the left) suggests sensitization. For downward shifts, each point on line B represents a higher rate of discharge (shorter interval) at an equivalent force. For leftward shifts, reactivity appears at forces which previously were ineffective.

tissue. In this instance, inflammation was induced at least 6 hours before recording began. Carrageenan (2%, 200 µl) was injected into the lateral and posterior aspects of the TMJ capsule as well as the superior joint space.

CHAPTER 3

RESULTS

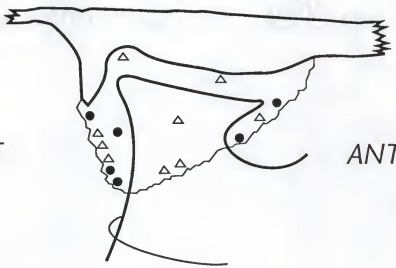
Identification of TMJ Nociceptors

Receptive fields for units with VP or HP reactivity were found on the lateral and posterior capsule of the TMJ (Figures 3-1 and 3-2). The mean von Frey thresholds for VP and HP units were 27 ± 39 g and 15 ± 20 g, respectively. The receptive fields of these units were single, small spots (approximately 2-3 mm). In some cases, receptive fields could not be identified. It is possible that the receptive fields of these units were located on the medial capsule, posterior attachment tissues or peripheral portions of the articular disc. Alternatively, it is possible that units without identified receptive fields were not of TMJ origin but, instead, of muscular origin (lateral pterygoid or temporalis muscles). Conduction velocities were determined to be in the group III and IV fiber range (0.4 to 8.5 m/s). Due to the inaccessibility of many of the receptive fields, conduction velocities could only be obtained for 30% of the units (19 of 63 units).

The response characteristics of TMJ afferents were examined. Mechanical reactivity to jaw movement was determined using both dynamically and statically applied forces. In order to distinguish between joint afferents acting as proprioceptors from those acting as nociceptors,we searched for afferents with a preference for intense stimuli. It was predicted that TMJ nociceptors would respond in the noxious range of mandibular motion, where the noxious range of motion was defined as that passive mandibular motion where the mandible encounters considerable resistance imposed by constraints of soft tissue.

Figure 3-1. Receptive field (RF) distribution in the lateral and posterior capsule of the TMJ for normal tissue. A) Distribution of RFs in the lateral capsule. B) Distribution of RFs in the posterior capsule. RFs (n=36) of afferents in A) and B) responded to either vertical plane (•) or horizontal plane (Δ) movement of the mandible. POST, posterior; ANT, Anterior; MED, medial; LAT, lateral.

A



B

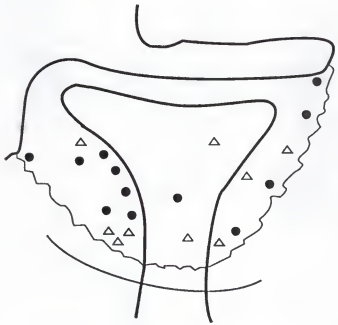
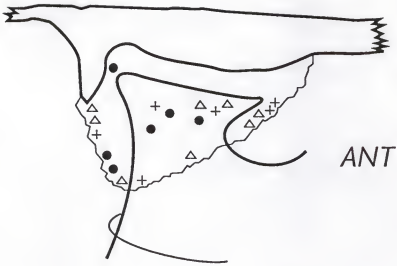
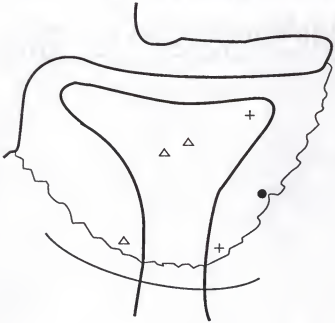


Figure 3-2. Receptive field (RF) distribution in the lateral and posterior capsule of the TMJ for previously inflamed tissue (•), acutely inflamed tissue (Δ) and saline control tissue (+). A) Lateral capsule. B) Posterior capsule. POST, posterior; ANT, anterior; MED, Medial; LAT, lateral.

A



B



Therefore, relationships between applied force and jaw movement were examined to determine the noxious range and compare it with afferent discharge properties.

Due to physical constraints of the preparation, force-movement relationships could only be examined for VP units. Characterization of force-movement relationships in the vertical plane revealed a biphasic relationship between applied force and mandibular movement (Figure 3-3). Linear force-movement relationships gave way to exponential force-movement relationships when the mandible reached an extreme of opening. It is likely that this exponential phase corresponds to the noxious range. Force-movement curves of VP units (n = 10) were best described by power functions (Table 3-1). Power functions were the best fit in 10 of 10 cases ($R^2 = 0.92 \pm 0.06$). The functional range of VP units may be graphically assessed by observing activation thresholds plotted on force-movement curves. As can be seen in Figure 3-3, nearly all afferents began to respond in the transition zone between the linear and exponential phases of the curves. This can be examined statistically by examining the functions fit below the point of activation. For the 10 cases in which power functions were fit, activation threshold occurred during portions of the curves which were exponentially accelerating (6/10 cases, $R^2 = 0.86 \pm 0.17$). In 4 cases, activation thresholds occurred in portions of the curve in which force was increasing linearly ($R^2 = 0.88 \pm 0.19$). The activation thesholds of these 4 units occurred at forces approaching the power phase of the curve. The observed preference for high forces (mean activation threshold for force = 20.6 ± 11.0 N; mean frequency asymptote = 49.6 ± 20.7 N) at extremes of the range of motion (mean activation threshold at $13.7^\circ \pm 5.4^\circ$; mean frequency asymptote = $20.4 \pm 5.9^\circ$) suggested that these TMJ afferents were nociceptors.

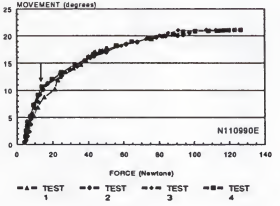
Characterization of TMJ Nociceptors in Normal Tissue

Units were classified according to their preferred movement plane. Preferred movement was defined as that plane of motion in which mandibular excursion evokes the

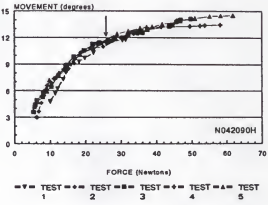
Figure 3-3. Relationships between applied force and vertical plane movements of the mandible. Ten biphasic curves indicated that low forces were sufficient to open the jaw through most of its range of motion. High forces produce minimal degrees of opening where the joint encounters considerable resistance from soft tissue. In each case, the TMJ nociceptor begins to respond at the point indicated by the arrow.

TMJ FORCE/MOVEMENT RELATIONSHIPS: VERTICAL PLANE

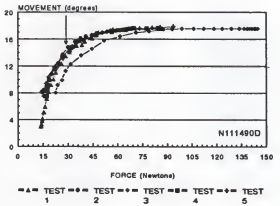
A



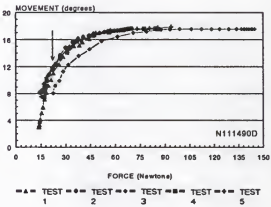
D



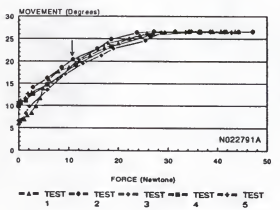
B



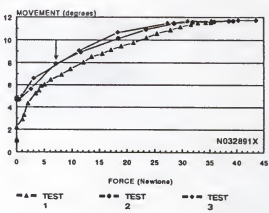
E



C

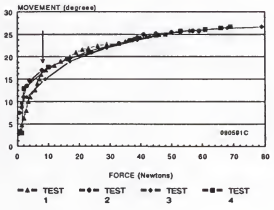


F

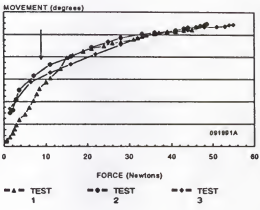


TMJ FORCE/MOVEMENT RELATIONSHIPS: VERTICAL PLANE

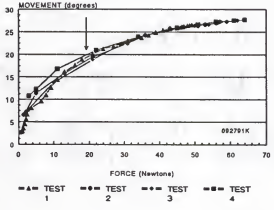
G



I



H



J

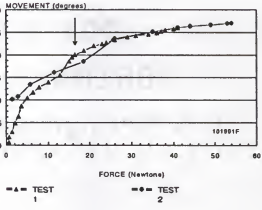


Figure 3.3. (cont'd)

Table 3-1

Force/Movement Relationships in the Vertical Plane

FILE	FUNCTION	FULL RANGE	LOW RANGE	R^2	P
042090H	POW	LnI = 0.69 LnF + 4.8		0.93	0.0001
042090H	LIN	I = 0.15 F + 1.8		0.90	0.0001
042090H	POW		LnI = 0.8 LnF + 0.89	0.96	0.0001
042090H	LIN		I = 0.2F + 0.87	0.95	0.0001
110990E	POW	LnI = 0.8 LnF + 2.1		0.97	0.0001
110990E	LIN	I = 0.6 F + 2.3		0.96	0.0001
110990E	POW		LnI = 1.1 LnF + 0.15	0.92	0.0001
110990E	LIN		I = 1.0 + 0.19	0.97	0.0001
111490D1	POW	LnI = 0.4 LnF + 1.1		0.91	0.0001
111490D1	LIN	I = 0.1F + 8.5		0.87	0.0001
111490D1	POW		LnI = 1.7 LnF + 2.2	0.92	0.0001
111490D1	LIN		I = 1.0F + 4.2	0.86	0.0001
111490D2	POW	LnI = 1.3 LnF + 1.2		0.91	0.0001
111490D2	LIN	I = 0.7F+ 0.22		0.87	0.0001
111490D2	POW		LnI = 2.3 LnF + 3.5	0.94	0.0001
111490D2	LIN		I = 1.4F + 7.4	0.97	0.0001
022791A	POW	LnI = 0.3 LnF + 2..2		0.93	0.0001
022791A	LIN	I = 0.77F + 11.0		0.79	0.0001
022791A	POW		LnI = 0.15 LnF +2.0	0.80	0.04
022791A	LIN		I = 1.8F + 5.9	0.97	0.0001
032891X	POW	LnI = 0.37 LnF + 1.1		0.99	0.0001
032891X	LIN	I = 0.23F + 3.7		0.88	0.0001
032891X	POW		LnI = 0.4 LnF + 0.01	0.98	0.0001
032891X	LIN		I = 0.55F + 2.3	0.88	0.0001
080591C	POW	LnI = 0.34 LnF + 1.9		0.87	0.0001
080591C	LIN	I = 0.28F + 12.0		0.77	0.0001
080591C	POW		LnI = 0.46 LnF + 1.8	0.57	0.0003
080591C	LIN		I = 1.5 F + 5.3	0.61	0.0001
091691A	POW	LnI = 0.54 LnF + 1.3		0.87	0.0001
091691A	LIN	I = 0.42F + 9.0		0.83	0.0001
091691A	POW		LnI = 0.64 LnF + 1.2	0.52	0.01
091691A	LIN		I = 2.3 F + 1.3	0.37	0.04
092791K	POW	LnI = 0.48 LnF + 1.4		0.96	0.0001
092791K	LIN	I = 0.37 F + 8.6		0.88	0.0001
092791K	POW		LnI = 0.59 LnF + 1.3	0.90	0.0001
092791K	LIN		I = .97F + 4.1	0.88	0.0001
101891F	POW	LnI = 0.5 LnF + 1.3		0.83	0.0001
101891F	LIN	I = 0.29F + 11.0		0.73	0.0001
101891F	POW		LnI = 0.74 LnF + 1.0	0.86	0.0001
101891F	LIN		I = 0.9 F + 5.6	0.64	0.0001

Note: POW, power; LIN, linear.

strongest response from an afferent. Thirty-six afferents with receptive fields in the TMJ capsule were activated by either vertical plane (VP or opening) or horizontal plane (HP or lateral displacement) motion. Eighteen afferents responded preferentially to movement in the vertical plane and 18 responded best to movement in the horizontal plane. A few units were activated by right lateral displacement (n = 5) or protrusive (n = 2) movement but most TMJ afferents responded preferentially to either opening (VP) or left lateral displacement (HP).

Once preferred movement was determined, tests of dynamic and static reactivity were conducted. Relationships between force, position or movement and response interval were quantified. The responses of TMJ nociceptors were quantified by regressions fit between instantaneous dynamic force, force velocity, movement, static force or position and instantaneous interspike interval.

As it was not clear which function would best describe TMJ afferents, linear, power, logarithmic and exponential models were explored. By comparison of the relative proportions of variance accounted for by each model, it was determined that power functions accounted for the greatest percentage of variance (mean $R^2 = 0.46 \pm 0.26$; n = 71 cases). Power functions were best fits compared to other functions for both dynamic (26/59 cases) and static tests (10/12 cases). Power functions were second best fits in 20 out of 59 cases for dynamic tests and 1 out of 12 cases for static tests. Linear functions were superior in 7 cases, logarithmic in 12 cases and exponential in 16 cases. Since power functions were the best or second best fit in 46 of 71 cases (mean $R^2 = 0.45 \pm .30$), power functions were used to represent the data in normal tissue. In inflamed tissue (both PI and AI), power functions accounted for the greatest percentage of variance in 101 of 146 cases (mean $R^2 = 0.50 \pm 0.21$).

TMJ nociceptors could be found which transduced (or coded) all aspects of force, movement or position, and many transduced more than one variable. "Code" indicates that

a unit's reactivity was proportional to force or some other stimulus variable and that the relationship could be described by a significant power function.

The great majority of TMJ nociceptors (n = 24) coded dynamic aspects of force applied to the mandible, and relatively few coded for static aspects of these stimuli. Twenty-three of 36 units that responded to either VP or HP jaw movement coded for dynamic force (mean activation threshold = 20.1 $\pm$ 17.5 N) and 15 of 36 units coded for force velocity (mean activation threshold = 15.5 $\pm$ 20.5 N/s; Table 3-2). In contrast, only 8 of 36 units coded for static force (mean activation threshold 17.8 $\pm$ 18.3 N), while 5 of 35 units coded jaw movement (mean activation thresholds of 11.0° $\pm$ 4.0°, and only 1 of 36 units coded for jaw position. In some cases, unit reactivity could be described by more than one function. Twelve of 23 units that could be fit to dynamic force were also significantly fit to force velocity. Six of these 12 units were significantly fit to force velocity, and 6 of these 12 units were signficantly fit to static force as well. Ten of 36 units could not be fit to any function. Fourteen additional units had jaw movement reactivity but no receptive field could be found.

Mean functions were generated from individually fitted functions by pooling slopes, intercepts and boundary values. Functions presented in Figure 3-4 represent the principle transducing properties of TMJ afferents: dynamic force and force velocity.

Properties of TMJ Nociceptors in Inflamed Tissue

The response properties of afferents were examined in capsular tissue that was previously inflamed (PI) by carrageenan. In these experiments, TMJ tissues were exposed to carrageenan for at least 6 hours prior to testing. In other experiments, afferents were tested in normal tissue and then tested again after an acute injection of carrageenan or saline. Afferent reactivity was examined for up to 3 hours subsequent to exposure to carrageenan.

TABLE 3-2

TMJ NOCICEPTOR REACTIVITY IN NORMAL TISSUE

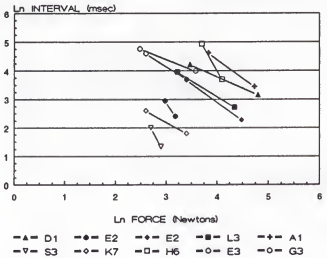
Test Conditions	with RF (n=36)		without RF (n=14)	
	code (n=25)	no code (n=10)	code (n=9)	no code (n=5)
Dynamic Force	23	12	6	6
Force Velocity	15	19	4	8
Movement	5	10	2	3
Static Force	8	23	1	4
Static Position	1	14	0	4
Conduction Velocity	0.4 to 7.5 m/sec (n = 6)	0.5 to 1.5 m/sec (n = 3)	.	.
Post-test Spontaneous Activity	3	0	0	0

Note: Receptive fields (RF) in the TMJ capsule were identified for 36 units. Twenty-five units with RFs coded for one or more of the stimuli. Most units (n = 23) with an RF on the TMJ capsule coded for dynamic force. Fourteen additional units had either VP or HP reactivity but an RF could not be found. "Code" indicates that a unit's reactivity could be described by a significant power function. Of the 36 afferents with RF's in the TMJ capsule, 3 units demonstrated spontaneous activity after dynamic or static testing. Five units with RF's in the TMJ capsule responded preferentially to right lateral displacement. Most of these units (3 of 5 cases) coded dynamic force. Appendix G contains descriptive statistics for these units.

Figure 3-4. Dynamic reactivity in normal tissue. Power functions best described the relationship between instantaneous dynamic force and force velocity with instantaneous response interval for afferents responding to mandibular movement in the vertical plane (VP) and horizontal plane (HP). A) Ten of 18 VP units transduced dynamic force (mean slope = -1.3 $\pm$ 0.2; range = 17.0 $\pm$ 33.5 to 48.5 $\pm$ 22.0 N; mean R^2 = 0.46 $\pm$ 0.21). These units were activated at a mean opening of 11.2 $\pm$ 4.4°. The range of activity of each nociceptor was defined as the smallest force or movement required to produce the minimum response frequency to the force of movement that produced the highest response frequency. B) Eight of 18 VP units transduced force velocity (mean slope = -0.6 $\pm$ 0.2; range = 17.5 $\pm$ 19.5 to 157.0 $\pm$ 86.0 N/s; mean R^2 = 0.30 $\pm$ 0.18). C) Thirteen of 18 HP units transduced dynamic force (mean slope = -0.9 $\pm$ 0.7; range = 9.7 $\pm$ 7.3 to 37.0 $\pm$ 22.8 N; mean R^2 = 0.39 $\pm$ 0.24). D) Seven of 18 HP units transduced force velocity (mean slope = -0.39 $\pm$ 0.24; range = 7.9 $\pm$ 16.9 to 166.0 $\pm$ 92.2 N/s; mean R^2 = 0.27 $\pm$ 0.14).

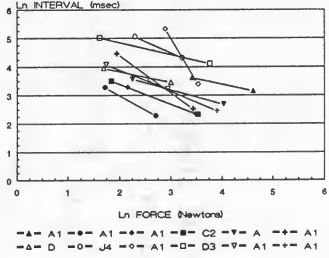
A

REACTIVITY IN THE VERTICAL PLANE:
DYNAMIC FORCE



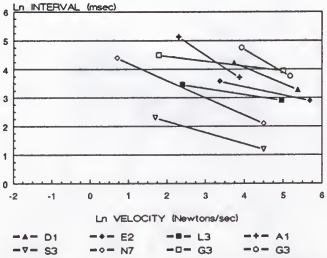
B

REACTIVITY IN THE HORIZONTAL PLANE:
DYNAMIC FORCE



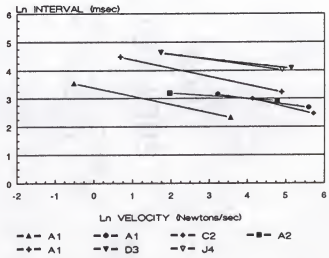
C

REACTIVITY IN THE VERTICAL PLANE:
FORCE VELOCITY



D

REACTIVITY IN THE HORIZONTAL PLANE:
FORCE VELOCITY



Experiment I: Properties of Units in the Previously Inflamed TMJ

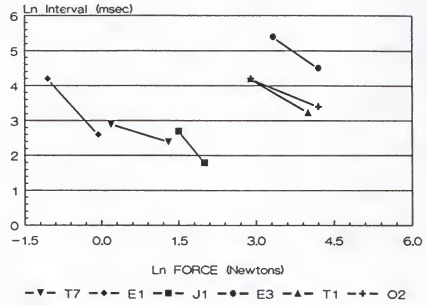
In the PI condition, transduction of the dynamic aspects of stimulus force was best described by power functions. Power functions were the best fit compared to other functions (7 of 13 cases; $R^2 = 0.33 \pm 0.25$) and were best or second best fit in 9 of 13 cases. Therefore, exposure to carrageenan did not modify the nature of functions which described afferent activity. Individually fitted power functions generated during dynamic and static response testing in inflamed tissue are illustrated in Figure 3-5.

Comparison of units in normal and inflamed tissue (see Figure 3-6) suggested improved reactivity for units that responded preferentially to movement in the vertical plane. Increased reactivity to dynamic stimuli was particularly prominent. In normal tissue, 11 of 18 units with RFs on the TMJ capsule coded for dynamic force or velocity; while proportionally more units (5/5) transduced dynamic force or velocity in the PI condition. Mean functions for dynamic force in inflamed and noninflamed conditions were calculated by averaging slopes and intercepts of individual functions (LnI = -1.3LnF + 7.3, (n = 25); LnI = - 1.1 LnF + 5.4, (n = 6)] for inflamed and noninflamed, respectively). The mean functions for all VP and HP units fitted during dynamic testing in normal and inflamed tissue suggested improvement of dynamic reactivity (Figure 3-6). The shifts of the mean function for units in PI condition to a graphic position below the mean function for normal tissue was suggestive of sensitization to dynamic forces.

Mean functions were also calculated for afferents transducing force velocity. A shift of the mean function of PI units that coded for force velocity [LnI = -0.7 LnF + 3.5, (n = 6)] was also observed in comparison to the mean functions in normal tissue [LnI = -0.38 LnF + 4.7, (n = 16)]. These functions are illustrated in Figure 3-6. A shift of the mean function for afferents in inflamed tissue below and to the left of the mean function for normal tissue also suggested sensitization to velocity of applied forces.

Figure 3-5. Dynamic reactivity in previously inflamed tissue. Power functions best described the relationship between instantaneous dynamic force and force velocity with instantaneous response interval in the vertical or horizontal plane. A) Six of 7 units transduced dynamic force (mean slope = -1.1 $\pm$ 0.5; range = 7.6 $\pm$ 10.2 to 33.3 $\pm$ 32.1 N; mean R^2 = 0.24 $\pm$ 0.16). B) Six of 7 units transduced force velocity (mean slope = -0.7 $\pm$ 0.8; range = 4.8 $\pm$ 4.5 to 40.2 $\pm$ 22.2 N/s; mean R^2 = 0.33 $\pm$ 0.28).

REACTIVITY IN PREVIOUSLY INFLAMED TISSUE:
DYNAMIC FORCE



REACTIVITY IN PREVIOUSLY INFLAMED TISSUE;
FORCE VELOCITY

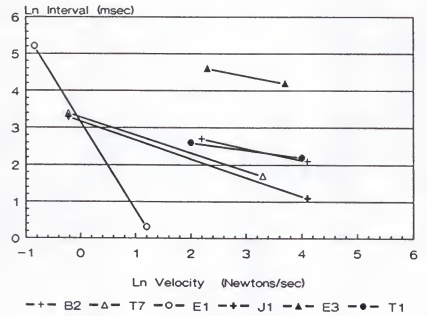
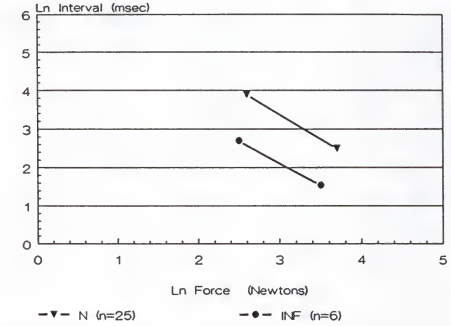
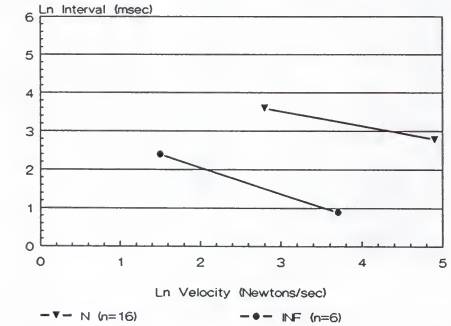


Figure 3-6. Averaged dynamic response functions of nociceptors fitted in normal and previously inflamed tissue (PI). A) Mean function for dynamic force fitted in PI tissue (mean interval = 29.9 $\pm$ 7.9 msec) falls below the mean dynamic force function fitted in normal tissue (mean interval = 44.7 $\pm$ 16.5 msec) suggesting sensitization. B) Mean function for force velocity in PI tissue (mean interval = 22.2 $\pm$ 3.3 msec; mean activation threshold = 17.3 $\pm$ 18.9 N/s) falls below and to the left of mean force velocity function fitted in normal tissue (mean interval = 7.4 $\pm$ 4.8 msec; mean activation threshold = 4.8 $\pm$ 4.5 N/s) suggesting enhanced reactivity (sensitization)

A CHANGES IN REACTIVITY TO DYNAMIC FORCE FOLLOWING CARRAGEENAN INFLAMMATION



B CHANGES IN REACTIVITY TO FORCE VELOCITY FOLLOWING CARRAGEENAN INFLAMMATION



Statistical comparisons between function characteristics in normal and inflamed tissues confirmed that dynamic reactivity improved in inflamed tissues (See Table 3-3). This was manifested as changes in activation threshold, frequency asymptotes and function intercepts. The mean activation threshold (8.3 $\pm$ 13.2 N) for units in inflamed tissue (n = 4) that responded best to jaw opening and transduced dynamic force was significantly lowered relative to the mean activation threshold (24.1 $\pm$ 11.2 N) for VP units (n = 10) in normal tissue ($F = 5.36$, $df = 13$, $p < 0.04$). For those same units, the mean intercept in inflamed tissue (5.0 $\pm$ 3.0) was significantly decreased relative to the mean intercept in normal tissue (9.0 $\pm$ 3.1). Similar changes were observed for afferents that transduced force velocity. The mean frequency asymptote (37.5 $\pm$ 23.6 N/s) for these units was significantly less than the mean frequency asymptote (148.0 $\pm$ 79.6 N/s) for units (n = 8), in normal tissue ($F = 8.89$, $df = 12$, $p < 0.01$). The mean force-frequency asymptote (40.2 $\pm$ 22.2 N/s) for PI units (n = 6) that coded for force velocity in both VP and HP jaw movements were significantly less than the mean force-frequency asymptote (156.5 $\pm$ 83.1 N/s) for VP and HP units (n = 15) in normal tissue ($F = 9.57$, $df = 21$, $p < 0.01$).

The changes we have observed in dynamic reactivity of TMJ nociceptors are suggestive of sensitization. However, experiments of this type (PI tissue) are subject to sampling errors. The best form of evidence for nociceptor sensitization comes from observations of single affferents making transitions from the normal to the sensitized state, following acute injections of pro-inflammatory substances.

Experiment II: Properties of Units in the Acutely Inflamed TMJ

The findings of enhanced dynamic reactivity observed in populations of afferents sampled from normal and subacutely inflamed TMJ tissues were complemented by observations made on units in which testing was performed before and after carrageenan-

TABLE 3-3. Mean values of properties of TMJ nociceptors.

A. NORMAL TISSUE

Test	n	Slope	Intercept	Act. Thres.	Freq. Asym.	Freg. Thres.	R^2	MRI
DF	23	-1.2 ± 0.9	7.3 ± 3.1	15.9 ±11.3	47.0 ±31.5	.	0.42 ±0.22	3.7±1.4
FV	15	-0.4 ± 0.3	4.8 ± 1.4	17.3 ±18.9	156.5 ±83.0	.	0.30 ±0.18	3.1±1.1
M	5	-4.2 ± 2.4	14.0 ± 6.7	10.8 ± 3.6	16.0 ± 7.5	.	0.49 ±0.23	9.9±4.8
SF	8	-1.6 ± 1.5	5.9 ± 2.4	17.7 ±18.3	42.5 ±26.5	7.9±7.9	0.75 ±0.23	3.6±1.5
P	1	-5.8	17	10°	16°	10°	0.73	6.6

B. PREVIOUSLY INFLAMED TISSUE

Test	n	Slope	Intercept	Act. Thres.	Freq. Asym.	Freg. Thres.	R^2	MRI
DF	6	-1.1 ±0.5	5.4±2.4	7.6±10.2	33.3 ±32.1	.	0.24 ±0.16	3.5±0.9
FV	6	-0.7 ±0.8	3.5±0.8	4.8± 4.5	40.2 ±22.2	.	0.33 ±0.78	2.2±1.3
M	1	-6.6	24	17°	20°	.	0.46	17
SF	2	-1.3 ±0.9	7.9±2.3	6.5± 3.6	25.5 ± 9.2	6.1±4.3	0.36 ±0.11	4.1±0.6
P	1	-2.0	10.0	10°	17°	7°	0.42	6.1

C. ACUTELY INFLAMED TISSUE

Test	Cond	n	Slope	Intercept	Act. Thres.	Freq. Asym.	Freg. Thres.	R^2	MRI
DF	Pre	9	-1.3 ±1.4	7.4 ± 4.1	12.9 ± 9.0	41.4 ± 13.3	.	0.43 ±0.23	4.3 ± 2.1
DF	Post	9	-0.9 ±0.6	5.5 ± 1.4	11.4 ±13.5	41.3 ± 24.9	.	0.38 ±0.20	3.2 ± 0.5
FV	Pre	2	-0.2 ±0.06	4.4 ± 0.57	14.0 ±18.4	252.0 ±114.6	.	0.39 ±0.07	3.0 ± 0.1
FV	Post	2	-0.7 ±0.7	5.6 ± 3.3	9.0 ± 5.7	167.0 ± 16.9	.	0.48 ±0.30	3.0 ± 0.1
M	Pre	3	-3.3 ±3.3	13.8 ± 9.9	15.7 ± 6.8	26.3 ± 2.5	.	0.40 ±0.08	7.8 ± 5.4
M	Post	3	-4.0 ±3.4	15.8 ±10.7	19.3 ± 7.2	24.5 ± 4.1	.	0.58 ±0.36	11.1 ± 9.5
SF	Pre	3	-1.0 ±0.6	7.4 ± 2.0	20.3 ±14.0	33.0 ± 13.9	8.2± 3.7	0.54 ±0.34	5.5 ± 2.1
SF	Post	3	-0.8 ±0.6	6.4 ± 2.2	8.5 ± 8.4	43.3 ± 11.7	5.2± 3.7	0.58 ±0.15	4.5 ± 0.7
P	Pre	1	-1.1	7.1	10.5°	16°	10°	0.35	5.2
P	Post	1	-1.2	6.8	3.4°	22°	2.7°	0.79	3.3

Note: DF, dynamic force; FV, force velocity; M, movement; SF, static force; P, position; Act. Thres., activation threshold; Freq. Asym., frequency asymptote; Freq. Thres., frequency threshold; R^2, coefficient of determination; MRI, mean response interval (natural log value).

induced inflammation (acutely inflamed or AI). Outcomes of experiments using PI methods suggested that individually characterized afferents would manifest improved dynamic reactivity.

Observations of quantitative shifts in force interval functions were confirmed, and additional qualitative changes were observed. Eleven units were characterized in normal tissue and then retested 1-3 h after exposure to carrageenan. Four units responded preferentially to VP jaw movement and 7 responded best to HP movement. For 9 units that transduced stimulus intensity in both normal and inflamed tissue, 6 demonstrated enhanced reactivity for dynamic force (Figure 3-7). Four of these 6 units had post-inflammatory functions that shifted below the pre-inflammatory function. One of these also showed leftward shift. Three of 6 units that demonstrated enhanced dynamic force reactivity showed a leftward function shift relative to pre-inflammatory functions but failed to shift below the control case. Mean function characteristics for these nociceptors are presented in Table 3-3.

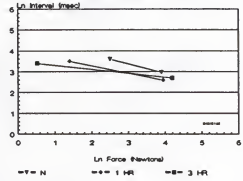
Experiments were performed to determine whether changes in AI reactivity occurred as a result of carrageenan or other causes, such as repeated stimulation. In these control experiments, saline (100 µl) was injected into the area of the RF and into the TMJ capsule. Reactivity was examined in 8 units after exposure to saline. Five of 8 units transduced dynamic force in both the pre- and post-saline conditions. While quantitative changes in reactivity were small following saline injections, there was some indication that repeated testing could produce qualitative changes in reactivity similar to those observed following carrageenan injection (See Figure 3-8).

Following saline injection, mean activation threshold was reduced from 14.1 $\pm$ 15.0 N in pre-saline condition to 11.5 $\pm$ 7.5 N . These changes were relatively small compared to changes observed following carrageenan (11.2 $\pm$ 9.9 to 5.1 $\pm$ 3.7 N). Statistical comparisons indicated that the mean changes in activation threshold was significantly less in saline than carrageenan treated cases ($T = -2.2$; $DF = 15$; $p = 0.04$)).

Figure 3-7. Demonstration of sensitization (enhanced reactivity). Six of 11 units were characterized in normal tissue and then tested again after acutely inflamed (AI) with carrageenan. Power functions generated from retesting in acutely inflamed tissue were positioned below and/or to the left of power functions fitted on normal tissue. N, normal, Min, inflamed; HR, inflamed.

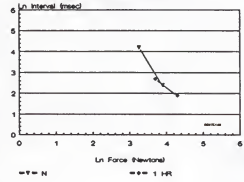
A

REACTIVITY IN VERTICAL PLANE: NORMAL TO INFLAMED
DYNAMIC FORCE: UNIT #1



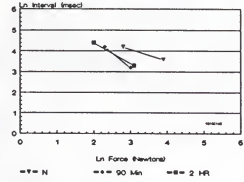
B

REACTIVITY IN VERTICAL PLANE: NORMAL TO INFLAMED
DYNAMIC FORCE: UNIT #3



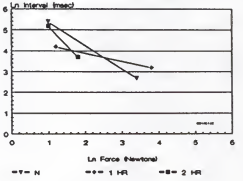
C

REACTIVITY IN VERTICAL PLANE: NORMAL TO INFLAMED
DYNAMIC FORCE: UNIT #4



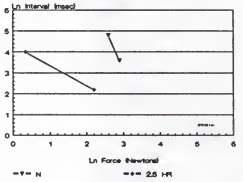
D

REACTIVITY IN HORIZONTAL PLANE: NORMAL TO INFLAMED
DYNAMIC FORCE: UNIT #2



E

REACTIVITY IN HORIZONTAL PLANE: NORMAL TO INFLAMED
DYNAMIC FORCE: UNIT #5



F

REACTIVITY IN HORIZONTAL PLANE: NORMAL TO INFLAMED
DYNAMIC FORCE: UNIT #6

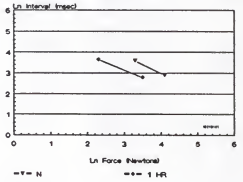
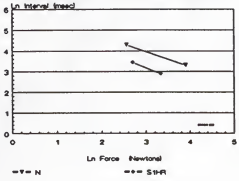


Figure 3-8. Reactivity of nociceptors exposed to saline. Five units transduced dynamic force in both the pre- and post-saline conditions. A) and B) demonstrate quantative changes in dynamic force reactivity. C), D) and E) show no enhanced reactivity.

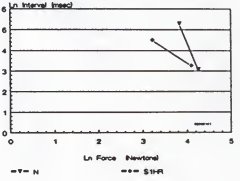
A

REACTIVITY IN HORIZONTAL PLANE: SALINE CONTROL
DYNAMIC FORCE: LEFT LATERAL UNIT #3



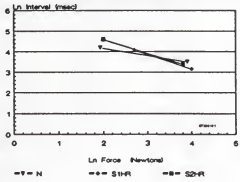
B

REACTIVITY IN HORIZONTAL PLANE: SALINE CONTROL
DYNAMIC FORCE: LEFT LATERAL UNIT #6



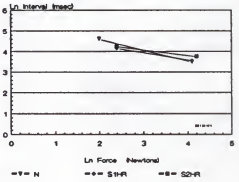
C

REACTIVITY IN HORIZONTAL PLANE: SALINE CONROL
DYNAMIC FORCE: LEFT LATERAL UNIT #2



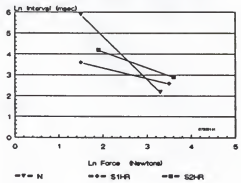
D

REACTIVITY IN HORIZONTAL PLANE: SALINE CONTROL
DYNAMIC FORCE: LEFT LATERAL UNIT #7



E

REACTIVITY IN HORIZONTAL PLANE: SALINE CONTROL
DYNAMIC FORCE: RIGHT LATERAL UNIT #1



Therefore while shifts in activation threshold could occur following repeated testing, the changes that followed carrageenan injection were significantly greater.

In experiment I, it was determined that most TMJ nociceptors transduced dynamic force and velocity, but few transduced either static force, movement or position. Following acute exposure to carrageenan, qualitative changes in coding capacities were noted; that is, afferents coded for stimulus features not previously transduced.

Qualitative improvements were observed for most units for either dynamically or statically applied stimuli. Eight of 11 nociceptors acquired either dynamic or static coding ability (Table 3-4). Four of 4 units that preferred VP jaw movement and transduced dynamic force in normal tissue acquired the ability to transduce force velocity ($n = 2$), static force ($n = 1$) or jaw position ($n = 1$) in inflamed tissue. Two of 5 AI units that preferred HP movement and transduced dynamic force in normal tissue also acquired the ability to transduce static force. Acquired coding also appeared in nociceptors that were without transducing capacity in normal tissue. Two of 7 AI units that preferred HP movement acquired the capacity to transduce both dynamic and static force. Other changes appeared as *de novo* reactivity. Three of 7 units that had only HP jaw movement initially acquired similar reactivity for VP movement (dynamic force). Six units demonstrated spontaneous activity after stimulus testing.

The finding that a large proportion (8/11) of nociceptors acquired coding ability after exposure of carrageenan suggested a qualitative form of sensitization. The nature of these qualitative changes can be best appreciated by comparing scatter plots representing comparisons between pre-inflamed and post-inflamed reactivity. Two types of trends (shift and rotation) were observed. Shift indicates a movement of a scatter of points into graphic zones of greater sensitivity. Rotation indicates the development of a significant slope associated with the scatter field of points. Of the 9 of 11 nociceptors that acquired coding ability, all 9 showed shifts and/or rotation. Figure 3-9 illustrates significant functions of units that demonstrated shifts and units that demonstrated rotation of scatter point fields.

Table 3-4.

EFFECT OF CARRAGEENAN ON TRANSDUCING CAPACITY

Qualitative improvements in reactivity for nociceptors that were characterized in normal tissue and then tested again subsequent to carrageenan injection. Eight of 11 nociceptors acquired either dynamic or static coding ability. Coding ability was also acquired for nociceptors (n = 2) that had no transducing capacity in normal tissue. Three units that responded to horizontal plane movement acquired vertical plane reactivity in acutely inflamed tissue. Six units demonstrated spontaneous activity after stimulus testing in acutely inflamed tissue.

UNIT	PLANE	PRE-INFLAMED	POST-INFLAMED	CODING SHIFT	OTHER MOVEMENT	POST-TEST SPONTAN. ACTIVITY
1	VP	DYNAMIC FORCE MOVEMENT STATIC FORCE POSITION	DYNAMIC FORCE FORCE VELOCITY MOVEMENT STATIC FORCE POSITION	YES	•	YES
2	VP	DYNAMIC FORCE	DYNAMIC FORCE STATIC FORCE	YES	•	YES
3	VP	DYNAMIC FORCE STATIC FORCE	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	YES	•	NONE
4	VP	DYNAMIC FORCE FORCE VELOCITY MOVEMENT	DYNAMIC FORCE MOVEMENT POSITION	YES	•	NONE

Note: VP, vertical plane

Table 3-4 (cont'd).

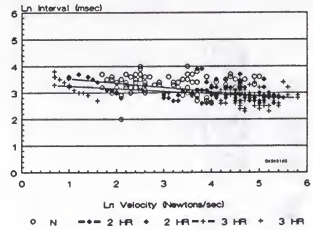
UNIT	PLANE	PRE-INFLAMED	POST-INFLAMED	CODING SHIFT	OTHER MOVEMENT	POST-TEST SPONTAN. ACTIVITY
5	HP	•	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	YES YES YES	•	YES
6	HP	DYNAMIC FORCE FORCE VELOCITY	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	YES	•	YES
7	HP	DYNAMIC FORCE FORCE VELOCITY	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	YES	OPEN: CODE OPEN: CODE OPEN: NON-CODE	NONE
8	HP	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	•	•	YES
9	HP	DYNAMIC FORCE	DYNAMIC FORCE	•	OPEN: CODE	YES
10	HP	DYNAMIC FORCE STATIC FORCE	DYNAMIC FORCE STATIC FORCE	•	•	NONE
11	HP	•	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	YES YES YES	OPEN: NON-CODE OPEN: NON-CODE OPEN: NON-CODE	NONE

Note: HP, horizontal plane

Figure 3-9. Comparison between pre-inflamed and post-inflamed reactivity in scatter plot forms. Two types of trends are displayed (rotation and shift). A,B,C and D) Units manifesting both rotation and shift to the left of scatter field. E,F,G.and H) Units manifesting rotation. Functions fit to scatter plots indicate significant transduction capacity was acquired. N, normal or pre-inflamed case; HR, hours afer carrageenan injection; M, minutes after carrageenan injection.

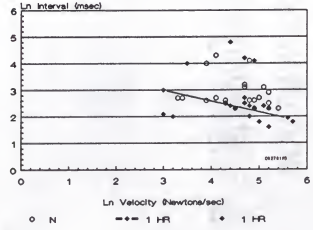
A

REACTIVITY IN VERTICAL PLANE: NORMAL TO INFLAMED
FORCE VELOCITY: UNIT #1



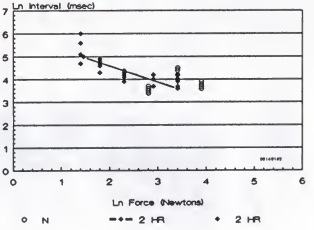
B

REACTIVITY IN VERTICAL PLANE: NORMAL TO INFLAMED
FORCE VELOCITY: UNIT #3



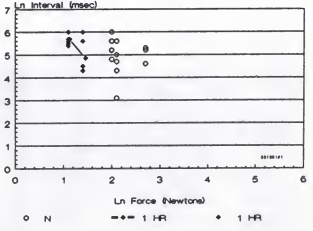
C

REACTIVITY IN HORIZONTAL PLANE: NORMAL TO INFLAMED
STATIC FORCE: UNIT #2



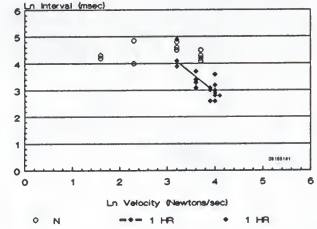
D

REACTIVITY IN HORIZONTAL PLANE; NORMAL TO INFLAMED
STATIC FORCE: UNIT #7



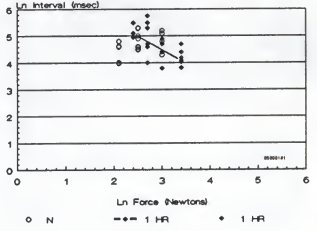
E

REACTIVITY IN VERTICAL PLANE: NORMAL TO INFLAMED
STATIC FORCE: UNIT #2



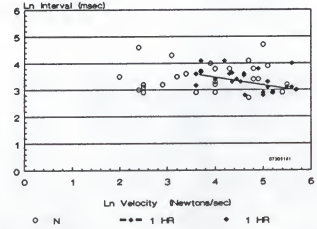
G

REACTIVITY IN HORIZONTAL PLANE: NORMAL TO INFLAMED
STATIC FORCE: UNIT #1



F

REACTIVITY IN HORIZONTAL PLANE: SALINE CONTROL
FORCE VELOCITY:LEFT LATERAL UNIT #2



H

REACTIVITY IN HORIZONTAL PLANE: NORMAL TO INFLAMED
STATIC FORCE: UNIT #3

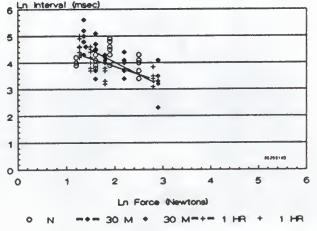


Figure 3-9. (cont'd)

Of the 9 units exhibiting rotation, 4 also shifted. It was possible that shift was a more mature form of sensitization that followed rotation. In units which were examined over several hours, 2 of 2 units that exhibited rotations subsequently manifested shifts of their scatter plot field (See Figure 3-9).

Control tests indicted that qualitative changes could also be observed after saline injection. In 1 of 8 cases, a qualitative improvement was observed in dynamic coding capacity (Table 3-5). Thus, improved dynamic reactivity is possible as the result of saline injection. However, the tendency towards acquired coding appeared to be greater for carrageenan-induced inflammation (8 of 11 cases).

In summary, experiments were performed to characterize the response properties of presumed nociceptors in normal and inflamed capsular tissue of the TMJ. Most TMJ afferents preferred either movement in the horizontal or vertical plane. Their reactivity functions were best described by power functions fit between dynamic force, force velocity and response interval. In normal tissue, TMJ afferents had properties of nociceptors, in that the activation threshold was at the extreme range of jaw movement, either in the exponential portion or in the transition zone between the linear and exponential force-movement curves that described jaw movement. It was predicted that TMJ nociceptors would sensitize following exposure to carrageenan. To test this, populations of afferents were sampled in previouslyly inflamed tissue and their responses compared to those of afferent populations in normal tissue. Improved reactivity was observed, especially reactivity to dynamic stimuli (dynamic force and force velocity). To avoid sampling errors that could have biased these observations, units were characterized in acutely inflamed tissue after being characterized in normal tissue. These afferents manifested similar quantitative improvements in dynamic reactivity. Additionally, qualitative improvements of coding capacity were observed. Acquisition of coding capacity following acute inflammation suggested afferent sensitization.

TABLE 3-5

EFFECT OF SALINE ON TRANSDUCING CAPACITY

UNIT	PLANE	PRE-CODING	POST-CODING	CODING SHIFT	OTHER MOVEMENT	POST-TEST SPONTAN. ACTIVITY
1	HP	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	•	•	NONE
2	HP	DYNAMIC FORCE STATIC FORCE	DYNAMIC FORCE FORCE VELOCITY STATIC FORCE	YES	•	NONE
3	HP	DYNAMIC FORCE STATIC FORCE	DYNAMIC FORCE STATIC FORCE	•	•	NONE
4	HP	DYNAMIC FORCE FORCE VELOCITY MOVEMENT STATIC FORCE POSITION	•	•	•	NONE
5	HP	NON-CODING	NON-CODING	•	•	NONE
6	HP	DYNAMIC FORCE	DYNAMIC FORCE	•	•	NONE
7	HP	DYNAMIC FORCE STATIC FORCE	DYNAMIC FORCE STATIC FORCE	•	•	NONE
8	HP	STATIC FORCE	STATIC FORCE	•	•	NONE

Note: Changes in reactivity for 8 units after exposure to saline. One of 8 units acquired coding ability for force velocity. HP, horizontal plane.

CHAPTER 4

DISCUSSION

Afferents were isolated from the trigeminal ganglion and efforts were made to determine whether they had nociceptive properties. Tests included quantification of response range, identification of relevant stimulus variables and the tendency to sensitize. Afferents that are nociceptors should transduce noxious stimuli (Sherrington, 1947), while other joint afferents (proprioceptors) would be expected to be most reactive in the normal range of motion, be bidirectionallly sensitive, and exhibit spontaneous activity (Burke et al., 1988; Macefield et al., 1990, Dorn et al., 1991).

The relationship between applied force and mandibular movement was examined to determine the "noxious range" and compare it with the threshold of afferents. The noxious range is likely to correspond to that portion of the force/jaw movement relationship where forces increased exponentially with jaw movement. TMJ afferents were activated at or near the beginning of the exponential phase and their firing became asymptotic in the exponential phase. Thus, a preference for high forces (mean activation threshold = 20.6 $\pm$ 11.0N) at extremes of the mandibular range of motion (mean activation threshold = 13.7 $\pm$ 5.4°; mean frequency asymptote = 49.6 $\pm$ 20.7 N) suggested that these TMJ afferents were nociceptors.

In contrast, a small group of units (n = 3) had responses to both jaw opening and closing. Their properties are distinct from populations of afferents which may be important in signalling tissue damage. Their activation thresholds (1.1 $\pm$ 0.9 N) and range of reactivity (1.1 $\pm$ 0.9 to 10.4 $\pm$ 4.1 N) are considerably different from that of nociceptors described above, and respond chiefly to innocuous joint movement within the physiological

range of motion. Afferents with similar properties have been observed in the cat knee joint (Dorn, et al., 1991). In this study, large diameter afferents (Group II) responded exclusively in the normal range of motion, were directionally sensitive, and demonstrated no resting activity. Whereas activity in nociceptors is likely to contribute to joint pain, these low threshold afferents may contribute to proprioception or sensations of pressure (Burke et al., 1988; Macefield et al., 1990; see Appendix B).

In other laboratories, recordings have been made from group III and IV joint afferents innervating the cat knee (Burgess and Clark, 1969; Clark, 1975; Schaible and Schmidt, 1983b). Schaible and Schmidt (1983b) divided their joint afferents into 4 subgroups which were differentiated, in part, by their qualitative response to movement. They defined nociceptors as those afferents that responded through, beyond or exclusively beyond the normal range of joint motion. These afferents had a steep rise in discharge frequency during forceful rotational movements, similar to those described previously (Burgess and Clark, 1969; Coggeshall et al., 1983). These observations compare favorably with ours, in that intense mechanical stimulation is needed to achieve a maximum response. It is difficult to make detailed comparisons between the response properties of afferents described by Schaible and Schmidt and others with those in our experiments, as no attempt was made by them to quantify the properties of afferents other than local pressure thresholds. Our experiments represent the first quantification of nociceptor reactivity across a range of suprathreshold stimuli with verification of the relationship between movement, response minima and maxima.

Early experiments created some confusion as to the basic properties of joint afferents. Studies that have examined the activity of mechanoreceptors supplying cat joint tissues (Burgess and Clark, 1969; Clark and Burgess, 1975; Rossi and Grigg, 1982) primarily emphasized proprioception, and addressed the questions as to whether position sense is coded by joint or muscle afferent fibers. They determined that joint afferents are only responsive at the extremes of the movement range, seemingly ruling out any useful

role in proprioception and clouding the functional distinction between free nerve endings (nociceptors) and well recognized encapsulated Golgi and Ruffini type end organs which are found throughout the capsule (Thilander, 1961; Ishibashi, 1966). Yet, others have reported that many afferents respond within the normal range movement (Klineberg et al., 1971; Lund and Matthews, 1981; Schaible and Schmidt, 1983b; Dorn et al., 1991). Microneurographic studies appear to have resolved this confusion in favor of the findings of Schmidt and company. These studies have examined the behavior of neuronal populations that signal joint position and mechanosensibility in humans. Burke et al., (1988) recorded responses of joint, muscle and cutaneous mechanoreceptors associated with finger joints to position and movement. Whereas most responded at the limits of joint rotation, a few afferents responded within the normal range. It is unclear whether the former group could code for pain, as pain was never induced by the movements, but the latter group appears to be appropriate for proprioceptive function. The relatively small population (3 of 16 cases) that provided a proprioceptive code was not dissimilar to our own (3 of 36 cases). Microstimulation of similar groups of joint afferents innervating finger joints indicated that innocuous sensations of movement or deep pressure were evoked (Macefield, et al., 1990). Thus, a proprioceptive role for joint afferents seems to be confirmed, although they may represent a small portion of the afferent population.

Sensitization of TMJ Nociceptors

Nociceptors in all preparations will sensitize following exposure to extreme heat (Burgess and Perl, 1967; Beck et al., 1974; Fitzgerald and Lynn, 1977; Campbell et al., 1979), mechanical forces (Reeh et al., 1987) or proinflammatory substances (Schaible and Schmidt, 1988a; Berberich et al., 1988; Cooper et al., 1991), and these are reflected as changes in central reactivity (Neugebauer and Schaible, 1990; see Appendix D). Sensitized nociceptors in skin, muscles and joints have enhanced reactivity to thermal, mechanical

and/or chemical stimuli. In our experiments, where afferents were sampled from previously inflamed capsular tissue or where characterized afferents were retested in acutely inflamed tissue, a variety of forms of sensitization was found. These changes included a significant decrease in mean activation threshold, shifts in stimulus response functions and qualitative forms of sensitization. Additional changes were observed for afferents in the PI condition (frequency asymptote and intercept) that were not replicated in the AI condition.

Recent experiments on cat knee joint nociceptors (Schaible and Schmidt, 1988b) have also produced evidence of changes in reactivity following carrageenan injection. Over half of the units that were classified as nociceptors in normal tissue responded to innocuous joint movements in the normal range of motion after inflammation. In effect, such enhanced reactivity, from extremes of movement to the normal range of motion indicates a decreased activation threshold. In our experiments, decreases in activation threshold were observed following carrageenean-induced inflammation. These decreased activation thresholds fell within the linear phase of force-movement relationship.

In our study, qualitative forms of sensitization were also observed. These appeared both in carrageenan treated nociceptors (8 of 11 cases), and infrequently in saline treated controls (1/8). The nature of these qualitative changes can be best appreciated by comparing scatter plots representing comparisons between preinflamed and postinflamed reactivity. It is important to examine scatter plots because the acquisition of transducing ability could have represented a distorted outcome. For example, outliers could have rendered functions insignificant where they were otherwise significant. However, examination of plots following carrageenan showed new relationships between force and response interval and shifts to greater reactivity.

Two types of trends were observed: rotation and shift. Rotational trends were indicated by a change in slopes which suggested increased proportional reactivity. A shift to the left represented a decrease in activation threshold that was seen consistently in AI and PI conditions for units with extant coding capacity. The shifts that were observed, were

less likely to be related to the development of qualitative changes than rotation. Rotation represents a new functional reactivity in the form of a proportional response to imposed forces. The basis of the qualitative changes could be either receptor based metabolic alteration secondary to the generation of proinflammatory substances, or could result from improved mechanical coupling between the receptor and the applied force.

Edema is a major component of inflammation that may impact on mechanical coupling. Afferent terminals of small fibers that are located in the area of inflammation are subject to an altered physical environment as a consequence of fluid extravasation. What effect local changes from edema may have in the responsiveness of joint receptors is unclear. In other preparations, edema may act to enhance or deter afferent responsiveness, the direction of the effect being dependent on tissue properties that are peculiar to each site (Cooper et al, 1990).

Acquisition of transducing capacity could be similar to observations of recruited activity described by other laboratories. This "recruitment" of afferents was observed in the cat knee joint preparation (Schaible and Schmidt, 1985, 1988b) and also in cutaneous preparations (Handwerker et al., 1991). A distinction between our observations and those of Schaible and Schmidt is that our sensitized afferents all have some pre-existing reactivity. We did not observe recruitment as silent units which "wake up." Given this, recruited activity and acquired coding may be distinct forms of sensitization. Our failure to observe recruitment may be due to methodological constraints of our preparation. In our experiments, extracellular recordings of neural activity in the trigeminal ganglion limits the number of neurons that could be recorded at any site. Very few cell bodies are in the functional range of the microelectrode. On the other hand, in teased fiber preparations such as those used by Schaible, Schmidt and Handwerker, electrodes have essentially zero impedance, therefore many more afferents can be recorded from simultaneously. This makes it more likely for recruitment to be observed.

Factors Contributing to Sensitization

Mechanical sensitization of joint afferents, following inflammation, is likely to be due to the production and release of endogenous substances. Injection of carrageenan produces a rapid inflammation that has been characterized in a number of behavioral and physiological preparations (Vinegar et al., 1987). Various factors may contribute to sensitization of joint afferents during carrageenan-induced inflammation, including both edema and the formation and release of algesics.

Changes in the response properties of joint afferents during inflammation have been attributed to the actions of bradykinin, prostaglandins, and serotonin. These mediators may alter mechanical responsivity of afferents, modify chemical responsivity, activate afferents or a combination of the three. Changes in reactivity of small fibers in inflamed tissue to bradykinin have been observed (Kanaka et al., 1985; He et al., 1990; Grubb et al., 1991). Bradykinin activates most group III and IV units that responded to passive joint movement. Bradykinin also activates afferents otherwise classified as "silent" (Heppleman et al., 1987).

Joint afferents can also be activated by prostaglandin (E or I). Prostaglandins E_1 or E_2 activated small afferents which responded to passive joint movement (Heppleman et al., 1985; Schaible and Schmidt, 1988a), and modified mechanical responses of these afferents. Following exposure to PGE_2, most group III and some group IV units showed enhanced joint movement reactivity and responded within the normal range of motion. These PGE_2-evoked increases in unit responsiveness paralleled those observed during acute arthritis (Schaible and Schmidt, 1985, 1988a). Similar properties have been prescribed for PGI_2, and it has been suggested that PGI_2 may be the dominant PG in joint afferent sensitization (Birrell et al., 1991; McQueen et al., 1991).

Interactions between pro-inflammatory mediators are also likely to be important, but they have not been determined in much detail. Prostaglandin E_1 (Schaible, 1983) and

prostaglandin E_2 (Grubb et al., 1991) have been shown to sensitize joint nociceptors to bradykinin. This may impact both on movement sensitive and tonic forms of joint pain.

Serotonin is also important in nociceptor sensitization. The effect of 5-HT on response characteristics of small afferent fibers have been studied in normal and inflamed cat knee joints (Heppelman et al., 1987) and rat ankle joints (Birrell et al., 1990; Grubb et al., 1988). Most group III and IV fibers that showed reactivity to cat knee movement were also activated by 5-HT. Units recorded from normal rat ankle joints were excited by 5-HT and showed enhanced activity in arthritic joints.

The consequences of carrageenan injections are very complex, and have not been determined for joints specifically (Vinegar et al., 1987). One sequence of events that occurs in skin, during the initial stage of inflammation (0-60 min) suggests a divergence from mechanisms proposed for sensitization of joint afferents. Immediately after injection of carrageenan, small amounts are absorbed by mast cells. The cytotoxic action of carrageenan initiates the arachidonate metabolic cascade and mast cell degranulation. Endoperoxides and serotonin are released. The endoperoxides are not believed to be prostaglandins but are believed to be reactive intermediates, and bradykinin is not believed to play a role. This stands in contrast to studies directly implicating bradykinin, PGE's and PGI_2 in afferent sensitization and at the very least implicates that additional factors may play a role in carrageenan inflammation. The role of 5-HT in carrageenan induced arthritis is also unclear. While 5-HT is released by carrageenan in rats, it is unlikely to be directly released in other species due to the absence of 5-HT in mast cells. Serotonin may be more important when vascular damage occurs (Zeller et al, 1983; Garcia-Leme, 1989). This may, in fact, be more relevant to TMJ dysfunction.

Clearly, reactivity to a host of algesics is shared by most small diameter afferents innervating joint tissue. Bradykinin, prostaglandins and perhaps 5-HT may play a role in afferent sensitization in inflamed joints. However, in each instance, it is not clear what is meant by normal range of motion and it is not clear to what extent shifts produced by

bradykinin, PGE_2 or serotonin are the basis for changes produced with carrageenan or other proinflammatory substances. The lack of detail in this respect is partly due to the absence of quantification of stimulus and response variables. Quantification of neural activity in respect to threshold, range and salient stimulus features (static or dynamic reactivity) should permit a fuller evaluation of role played by these substances and others in modification of joint nociceptor reactivity.

APPENDIX A

DEVELOPMENT AND MAINTENANCE OF TMJ PAIN

Many theories have been advanced to account for the production of TMJ pains. (For reviews, see Deboever, 1973; Dubner et al., 1978, Yemm, 1979). TMJ dysfunction may account not only for pain in the joint itself, but also for pain arising from associated facial structures.

Intra-articular Origins of TMJ Pain

1) Pressure Theory

Pressure theories have been the most prevalent explanations for the production of TMJ pain. These theories suggest that disruption of the normal articular mechanics may impose abnormal pressures on structures of the TMJ. Costen (1934) postulated that facial pain associated with the TMJ was a consequence of pressure on the auriculotemporal nerve brought about by impaction of the condyle against the tympanic plate. Anatomically, this theory is untenable since the auriculotemporal nerve ramifies before reaching the TMJ. The articular branches of the auriculotemporal nerve arise at the medialposterior aspect of the neck of the condyle and ascend into the soft tissue of the joint inferior to the tympanic plate.

The auriculotemporal nerve is vulnerable to pressure at its proximal course. The auriculotemporal nerve arises from the posterior trunk of the mandibular nerve along the medial surface of the lower belly of the lateral pterygoid muscle. Entrapment of the auriculotemporal nerve in the lateral pterygoid muscle has been demonstrated in 5% of

cadaver specimens (Loughner et al., 1990). Pressure in the form of compression by a hyperactive lateral pterygoid muscle may produce pain and/or paresthesia. Furthermore, patients with an internal derangement of the TMJ often have accompanying spasticity of the lateral pterygoid muscle.

Pressure on the posterior attachment tissues by the condyle could also cause TMJ pain (Sicher, 1955). Posterior displacement of the condyle or spastic contracture of the superior belly of the lateral pterygoid muscle may result in anterior displacement of the disc. As a consequence, the posterior attachment tissues are positioned where forces generated during mastication may produce local pressure on these highly vascularized and innervated tissues.

Local joint pressure may activate mechanoreceptive nociceptors in connective tissue such as the posterior attachment tissues. Inflammation could result from trauma due to a sudden, intense impact or from repeated pressure. Endogenous algesics released in the zone of inflammation may sensitize joint nociceptors by decreasing threshold and increasing response to mechanical stimuli (Heppelman et al., 1985).

A common procedure thought to discern anterior displacement of the disc is the impact-loading test. Manual loading applied in an anterior-superior direction at the posterior portion of the body of the mandible impacts the condyle into the articular fossa. If pain is evoked, it is thought that the disc is displaced and the condyle is impacting onto the posterior attachment tissues. However, disc displacement may exist without impact loading pain. This is assessed by imaging techniques, such as arthrography or magnetic resonsance imaging. Therefore, direct pressure on the disc or posterior attachment tissues is not sufficient to explain TMJ pain in all cases.

A corollary notion related to Sicher's theory was advanced by Frost (1968) to explain some patterns of joint pain. Frost hypothesized that bone pain may be evoked by the pressure of two articulating, irregular, joint surfaces in the absence of an intact interposing disc. Presumably, the irregular bony surfaces represent osteoarthritic changes.

Other investigators (Kreutziger and Mahan, 1975) have included arthroses of bony structures as causative factors in TMJ pain. Besides the degenerative processes that may occur in the bony anatomy of the TMJ, degenerative changes of the villi of the synovium have been claimed to be causally related to TMJ pain (Olson, 1969). Supposedly, disruption of the secretory function of the villi can disturb proper nutrition and lubrication of the TMJ resulting in TMJ dysfunction.

2) Tension Theory

Tension theories of TMJ pain can be divided into static and dynamic. Static state involves a resting position of the mandible. Dynamic state involves active or passive jaw movement. Anteriormedial displacement of the disc may generate static tension on the posterior and lateral aspects of the capsule (Dubner et al., 1978) where the greatest member of mechanoreceptors are located (Zimny, 1988). It is possible that resting tension will produce prolonged discharge in TMJ nociceptors. If the anteriormedial displacement of the disc is advanced, there is a release of the disc attachment at the lateral pole of the condyle which untethers the disc from the lateral aspect of the TMJ. In this case, the posterior attachment tissues are vulnerable to tension from a disc displacement during static conditions.

Patients suffering from pain in the TMJ often demonstrate symptoms of capsulitis; this included pain on local palpation or pain during small movements within the normal range of motion. Inflammatory processes in the TMJ may initiate or potentiate TMJ pain (Dubner et al., 1978). Dynamic theories propose that pain is produced during jaw movement by excitation of functionally distinct types of mechanoreceptors in the capsule and posterior attachment tissues. Activation may be enhanced by capsulitis. Zimmy (1988) advanced a conceptual model of TMJ pain during jaw movement. As the condyle rotates and translates freely through intermediate degrees of angle, the capsule and posterior attachment tissues are deformed. Such deformation is normally insufficient to excite mechanoreceptors. As the condyle approaches its border movement, the capsule and

posterior attachment tissues become taut. Mechanoreceptors in the capsule and posterior attachment tissues are activated by the resultant tension. Thus, these mechanoreceptors appear to act as detectors that sense the safe limits of joint movement. Supposedly, jaw movement beyond safe limits can represent real or potential tissue damaging stimuli. If these mechanoreceptors are nociceptors, they may be sensitized following capsulitis so that small movements in the functional range of motion produce pain. Clark and Burgess (1975) suggested that large, myelinated afferents signal the pressure felt as the extremes of joint movement are reached. These investigators demonstrated that slowly adapting receptors in the capsule were excited only at extremes of flexion and extension of the knee joint of the cat (Burgess and Clark, 1969). On the other hand, Schaible and Schmidt (1983b) attribute a similar detection role for small fibers which are active only at the borders of the joint movement.

Following capsulitis, the tension required to produce activation of nociceptors might be greatly reduced. Animals studies in the cat knee joint (Schaible and Schmidt, 1988b) and rat ankle joint (Guilbaud, 1988) have demonstrated increased responsiveness of group III and IV afferents to innocuous mechanical stimulation after induction of acute inflammation . The relationship between nociceptor discharge and capsular tension is yet to be demonstrated.

The reactivity of mechanoreceptors in the capsule of the cat knee have been used to assess tension produced by joint movement (Grigg and Hoffman, 1989; Hoffman and Grigg, 1989). The frequency of neurons with receptive fields in the posterior capsule showed a linear relationship with tension applied (knee extension) at the area of the receptive field. The posterior joint capsule was minimally loaded even during hyperextension movements.

Extra-articular Theories of TMJ pain

Distinct theories of the origin of extra-articular pain have arisen, and include the myofascial pain theory and referred pain theory.

1) Myofascial Pain Theory

The myofascial pain theory postulates chronic hyperactivity in head and neck musculature as a causative agent in extra-articular pain. The myofascial pain theory suggests that the chronicity of muscle pain is due to the "trigger point" (Travell, 1976). The trigger point is defined as a localized area of chronic inflammation of fibrous connective tissue in muscle. Histological examination of biopsy material from trigger points in patients suffering from interstitial myofibrositis reveal degranulated mast cells and platelet clots (Awad, 1973). The author proposes a hypothesis suggesting that trauma-induced extravasation of platelets leads to release of 5-HT which subsequently results in edema and vasoconstriction. The release of such endogenous algesics in muscle may play a role in the pain and tenderness associated with trigger points. For example, activation of group IV afferent neurons in cat muscle have been demonstrated by close arterial injection of bradykinin, 5-HT or histamine (Mense and Schmidt, 1974). Serotonin may also sensitize mucosal nociceptors to mechanical stimuli (Friedman et al., 1988; Cooper et al., 1991).

Muscle pain and the reduction of pain free jaw movement are frequent complaints of patients with facial pain. The limitation of jaw movement may involve the modulation of the reflex control of masticatory muscles (Klineberg, 1971; Dubner et al., 1978). Greenfield and Wyke (1966) studied the role of TMJ afferents in reflexes that modify the activity of muscles of mastication. The experimental procedure involved detaching all the supra- and infra-mandibular muscles at their insertions from one half of the cat mandible. Movement of the ipsilateral half of the mandible resulted in activation or inhibition of

dissected muscles. Similar responses were produced in the detatched muscles by direct tension on the capsule after condylectomy.

Jaw movement has been shown to modulate the firing pattern of alpha motoneurons in the trigeminal motor nucleus in cats (Kawamura et al., 1967). These investigators demonstrated changes in the discharge rate of motor neurons of the masseter muscle in response to passive rotation of the ipsilateral condyle. Rotating the condyle to an open position evoked an increase in firing pattern of masseter motoneurons. A closed position evoked a decrease in firing pattern.

Abe and Kawamura (1973) recorded efferent discharges from branches of the mandibular nerve which innervate the masseter and digastric muscles. Ipsilateral condylar rotation to an open position inhibited alpha-motor units in the masseteric nerve. Local mechanical stimulation of the posterior part of the TMJ capsule inhibited the discharge pattern of masseteric neurons and facilitated motor fibers innervating the digastric muscle. It is not surprising that afferent activity from mechanoreceptors in the TMJ modulate efferent activity in masticatory muscles in order to coordinate jaw movement. The presence of chronic activation of TMJ afferents may induce chronic reflex activation of facial musculature. Chronic activation may produce muscle pain that limits movement.

Clinically, bruxism has been associated with muscle hyperactivity and TMJ dysfunction. Bruxism is defined as a nonfunctional voluntary or involuntary mandibular activity featuring habitual grinding or clenching of the teeth (Kawamura, 1980). Chronic, repetitive mandibular movement seen in bruxism is thought to deliver excessive reaction forces to the TMJ which could produce local inflammatory changes. Putative causes of bruxism include occlusal stress, CNS and hereditary factors.

2) Referred pain theory

Pain may be referred to the TMJ from other head and neck regions (Bell, 1969). Travell (1976) suggested that continuous hyperactivity of muscles from the head and neck may refer pain to the TMJ. The explanations for the origin of referred pain have largely

ruled out nerve branching in the periphery as a source of referred pain. The convergence theory of referred pain invokes a central locus of action in the superficial layers of the medullary dorsal horn. Noxious input from different sources converge on transmission cells responding to noxious input (for review, see Fields, 1987). Pain may be mistakenly mislocated to an area distant from the site of origin due to expectation or previous experience with pain in the referred site.

In most cases, TMJ pain is not restricted to the joint but is also associated with extra-articular regions. The most common areas are ipsilateral eyeball, superciliary ridge, deep masseter muscle, and angle of mandible (Mahan and Alling, 1991). The craniovertebral junction and upper neck are other referral sites of TMJ pain (Schellhas et al., 1989).

APPENDIX B

PSYCHOPHYSICS OF TMJ DISORDERS

Pain and mandibular dysfunction are two common manifestations of TMJ disorders. Pain can occur when the mandible is at rest or during function. Disordered movement of the mandible is a sign of mandibular dysfunction (i.e. the inability to masticate properly). Patients suffering from TMJ disorders often complain of pain while chewing. Whether mandibular dysfuntion is directly or indirectly due to TMJ disorder or due uniquely to pain that results from jaw movement is unclear.

Chewing efficiency, jaw movement, biting force and perception of jaw position are quantifiable features of mastication. A review of the literature reveals studies which have been directed at investigating the relationship betwen TMJ disorders and mastication. There has been little psychophysical experimentation involved in quantifying pain associated with mandibular dysfunction. Even though most of these studies pertain to treatment efficacy, understanding the relationship between TMJ disorders and mastication may be valuable in understanding the relationship between pain and TMJ disorders.

Chewing Efficiency

Typically, the clinical appraisal of individual's chewing efficiency is limited to a subjective report provided by the patient. Early investigators (Christiansen, 1922; Dahlberg, 1942) developed the technique of using a series of sieves with different mesh sizes and test materials for chewing in order to estimate chewing efficiency. A simple

method that can be used clinically to assess chewing efficiency was developed by Loos (1963) and modified by Carlsson and Helkimo (1972). Test material is chewed for 10, 20 or 40 seconds.

Masticated test materials are then measured in millimeters. Chewing efficiency is rated according to the size of the material and number of seconds of chewing.

A more elaborate, standardized measure of chewing efficiency, called the Coefficient of Masticatory Performance, was developed by Manly and Braley (1950). The Coefficient of Masticatory Performance was defined as the percentage of chewed peanuts that pass through a 10-mesh screen sieve after being subjected to 20 masticatory strokes. Rominger and Rugh (1986), utilizing this test, compared the chewing performance of a group of patients with TMJ dysfunction to a group of normal controls. The patient group had significantly lower coefficient scores than the normal control group. Lemke et al. (1987) investigated the level of masticatory efficiency of post-TMJ surgical patients several years after treatment. These investigators found that the post-surgery group had significantly lower chewing efficiency scores than a group of non-treated non-dysfunctional patients.

Taken together, these studies indicate a negative relationship between chewing efficiency and TMJ disorders. Whether the inability to chew efficiently is due to the TMJ pain or associated muscular pain is uncertain.

Jaw Movement

The sensory apparatus of the TMJ is thought to play a role in the synchronizing mechanisms involved with the control of jaw movement (Sicher, 1955). The influences of TMJ afferents on functional jaw movements has been studied in both normal subjects and patients suffering from TMJ disorders. In normal subjects, Posselt and Thilander (1965) anesthetized the lateral part of the TMJ capsule. They observed an increase in lateral

movement and maximum opening. The authors suggested that the lateral ligament may be associated with a protective mechanism during extreme opening. Klineberg (1980) also anesthetized the TMJs of normal subjects and observed an increase in size of the envelope of function (range of motion), and suggested that mechanoreceptors of the TMJ play a modulatory role in motor control of the mandible.

One measure of jaw movement is maximum range of motion (ROM). The measurement is made for opening, lateral and protrusive excursions. An assessment of ROM for normal subjects has been reported by Posselt (1968). For normal subjects (adult males) maximum opening averages 50-60 mm; hinge opening, 20-25 mm; lateral excursion from midline, 10 mm; and protrusive excursion, 10 mm. Anaesthesization of the lateral capusle of the TMJ increased hinge opening and protrusion by 10-15% (Posselt and Thilander, 1965). For patients suffering from TMJ disorders, ROM is generally limited compared to normal subjects. Helkimo (1974) devised a pain-dysfunction index which rates severity of mandibular function in regard to pain report for jaw movement and TMJ palpation. This index was modified by Zarb and Carlsson (1988). Normal ROM was >39 mm for opening and >6 mm for lateral excursions. For patients, ROM was 30-39 mm for opening and 4-6 mm for lateral excursions. Patients with this amount of impairment reported pain during at least one jaw movement and pain on palpation of the TMJ's. For other patients, ROM was <30 mm for opening and <4 mm for lateral excursions. Patients with this amount of impairment reported during 2 or more jaw movements and pain on palpation of the TMJ's.

Many clinicians observe a decrease in ROM for patients suffering from TMJ disorders. These patients are often hesitant to open their mouth maximally because of real or expected pain. As a result, a measure of ROM may result in a value less than the patient is actually capable of producing. Therefore, other components of mastication may be more likely to be reliable measures of jaw function. Moreover, the movements of the mandible

that are made during mastication are well within the border movements of the mandible as defined by the ROM (Okeson, 1989).

Jaw Position

One feature of mandibular function is the ability to control the position of the mandible within the limits of one's maximum ROM. An important question in the literature dealing with proprioception is whether position sense is signalled by joint or muscle afferents. Part of the literature implicates joint afferents (For reviews see Rose and Mountcastle, 1959; Skoglund, 1973; Dubner et al., 1978); another part of the literature implicates muscle afferents (for review, see Burgess et al., 1982). It is reasonable to explain joint position sense in terms of both joint and muscle afferent input.

Jaw position sense has been studied in both normal subjects and patients suffering from TMJ disorders. Thilander (1961) assessed perception of mandibular position before and after unilateral or bilateral anesthetization of the TMJ in normal subjects. The results showed that subjects had more difficulty returning to an initial jaw position, following anesthetization. Larsson and Thilander (1964) explored the relationship between position sense and local mechanical pressure applied to the TMJ in normal subjects. The authors found that position sense was not influenced by local pressure. When the local pressure was reported to be painful, again position sense was not affected. However, when the joint was locally anesthetized, jaw position sense deteriorated. If then, local pressure was applied to the joint during the course of anesthesia, position sense returned to normal levels. Presumably, local pressure recruited muscle afferents. Input from muscle mechanoreceptors may have provided the sensory feedback necessary to restore position sense. The authors reported that ansethetization of the TMJ was performed by infiltration into the skin and tissues lateral to the capsule. This technique may have not anesthetized the TMJ completely.

Interdental thickness discrimination is one method that has been used to analyze the position sense of the mandible. Interdental thickness discrimination is the ability to detect differences in the thickness of test materials placed between opposing teeth. Caffese et al., (1973) studied the possible influence of TMJ receptors in tactile occlusal perception by assessing minimal thickness detection between opposing teeth before and after anesthetization of the TMJ. These authors found significant differences in threshold detection in the anesthetized joint compared to the normal joint. On the other hand, Siirila and Laine (1972) obtained different results from their study of interdental thickness discrimination. Anesthetization of TMJ did not significantly diminish subjects' ability to detect differences in thickness between teeth at various degrees of mouth opening. Morimoto and Kawamura (1978) obtained similar results and suggested that the muscle spindles in the muscles of mastication are mainly responsible for size discrimination.

If mechanoreceptors of the TMJ play a role in jaw position sense, their influence may be modulated by TMJ disorders. Ransjo and Thilander (1963) studied position sense of the mandible in patients with TMJ disorders which were thought to be of myogenic origin or due to functional malocclusion. The authors assumed that functional malocclusion caused impairment of TMJ receptors. Position sense was found to be poorer for the malocclusion group compared to the normal group. Position sense of the myogenic group was normal. Amelioration of TMJ symptoms after treatment was accompanied by improvement in the perception of jaw position. This study is in accord with the previous work of Thilander (1961) suggesting that TMJ mechanoreceptors play a major role in the ability to perceive position sense of the mandible.

A more recent study by van Willigen et al., (1986) investigated perception of jaw position in subjects with symptoms of TMJ disorders. They found that all subjects with craniomandibular dysfunction demonstrated greater mismatches of jaw position compared with normal subjects. On the other hand, other studies present contrasting evidence (Christensen and Troest, 1975; Morimoto and Kawamura, 1978; Broekhuijsen and van

Willigen, 1983; van der Berghe et al., 1987). Morimoto and Kawamura (1978) tested interdental thickness discrimination in 8 patients with unilateral or bilateral mandibular condyles that were either surgically mobilized or removed. The authors failed to observe any lessened capacity to discriminate thickness. These authors concluded that TMJ receptors were not essential to size discrimination ability.

Broekhuijsen and van Willigen (1983) studied position sense of the mandible in normal subjects before and after injection of the TMJ capsule bilaterally with local anesthetic. Perception of mandibular position was unaffected by anesthetization of the TMJs. Van den Berghe et al., (1987) assessed position sense of the mandible in patients suffering from TMJ disorders before and after treatment. Patients' abilities to determine jaw position were unchanged after successful treatment.

The relative unimportance of joint afferents in assessing position and movement is noted for a variety of joints. In the human knee joint, injection of local anesthetic into the joint does not deteriorate the subjects' ability to detect passive angular displacements of five degrees (Clark et al, 1979). Moreover, total joint replacement of the hip produces little impairment of sensations associated with joint movement (Grigg et al, 1973).

In summary, the ability to control the position of the jaw is an important aspect of mandibular function. Position sense has been studied in both normal subjects and patients suffering from TMJ disorders. The preponderance of the evidence suggests that sensory input from the TMJ contributes little information in controlling the position of the mandible.

Bite Force

Different parameters of bite force, such as maximum bite force, submaximal bite force and bite force discrimination have been investigated in an effort to assess mandibular function.

Maximum Bite Force

The maxmum bite force is the measure of the greatest force which an individual can produce by biting on an instrument containing a force transducer. The maximal level of bite force that an individual is capable of producing is rarely required or utilized during chewing. Therefore, the relevance of maximum bite force as a measure of mandibular function is uncertain. Also, a measure of maximum bite force may result in a value less than an individual is capable or willing to produce. Clark et al., (1984) reported that the maximum bite force of normal subjects is limited by pain tolerance. Patients suffering from TMJ disorder may be incapable of producing maximum bite force due to the direct effect of mandibular dysfunction or unwillingness to bite normally due to the indirect effect of pain. Such may be the case in several studies that assessed maximum bite force in patients suffering from TMJ disorders (Helkimo et al., 1975; Sheikolelam et al., 1982). Helkimo et al. (1975) reported that maximum bite force was lower in a patient group with TMJ disorders than for a control group. Patients' level of maximum bite force increased following treatment. Sheikolelam et al., (1982) observed that maximum bite force was significantly less for their patients with TMJ disorders than for normal controls.

Submaximal Bite Force

One important component of the normal chewing cycle is the individual's ability to produce and control relatively low levels of biting force. Submaximal bite force is the measure of different levels of biting force below maximum bite force. It seems reasonable to suggest that impaired mandibular function may result in impairment of the ability to control submaximal bite force. Several studies have investigated submaximal bite force in patients with mandibular dysfunction (Helkimo et al., 1975; Agerberg, 1988). Bite force was registered with different types of bite beams incorporating a force transducer. A common feature of patient populations was pain in the TMJ. These studies reported that

patients had lower values for submaximal bite force (3-25 kg) compared to control subjects (5-50 kg).

Bite Force Discrimination

In order for an individual to control the different levels of bite force, he/she must be able to discriminate differences in the intensity of their own biting force. The role of TMJ mechanoreceptors in bite force discrimination has been investigated in normal subjects (Williams et al., 1984; Williams et al., 1989). Bite force was assessed before, during and after anesthetization of the TMJ by auriculotemporal nerve block (Williams et al., 1984) or infiltration into the superior joint cavity (Williams et al., 1989). These studies suggest that the TMJ mechanoreceptors do not appear to be responsible for discrimination of bite force.

In summary, maximum bite force, submaximal bite force and bite force discrimination are three commonly used measures of mandibular function. Studies assessing maximum and submaximal bite force indicate that patients suffering from TMJ disorders have decreased bite force strength. The ability to discriminate bite force levels has not been studied in patients having TMJ disorders. Neither maximum bite force, submaximal bite force nor bite force discrimination measures have provided clear information on the relationship between TMJ sensory input and mandibular function.

APPENDIX C

NEUROANATOMY OF THE TMJ

Until Thilander's (1961) comprehensive, anatomical and histological study of the innervation of the human TMJ, research on innervation of the TMJ involved macroscopic studies. Rüdinger (1857) observed that the auriculotemporal nerve coursed to the posterior aspect of the joint where three or four articular branches entered the capsule. The anterior aspect of the capsule received one or two twigs derived from the masseteric and deep temporal nerves. Textbooks describing the TMJ generally accepted Rüdinger's findings. Moreover, other anatomists (Guerrier and Bolonyi, 1948; Baumann, 1951; Hromada, 1960) are in agreement with the neural topography described by Rüdinger but for the possible exception of the contribution of the facial nerve.

Some sensory fibers travel in the facial nerve, which is otherwise devoted to motor function. These afferent fibers constitute about 15% of the total nerve fiber population (Foley, 1960). Guerrier and Bolonyi (1948) reported that branches of the facial nerve always terminated in the lateral surface of the TMJ. Hromada (1960) stated that a twig from the facial nerve passed into the lateral aspect of the capsule in about half of his dissected specimens. On the other hand, Thilander (1961) reported that, immediately lateral to the capsule, a twig from the facial nerves courses in an anterior direction but does not ramify into the joint. Kerr (1962) also reported that afferents of the facial nerve terminate only in the dermatomes of C1 and C2 in the cat. Our observations (unpublished) suggest that the facial nerve does not innervate the TMJ of the human. However, the facial

nerve was seen to communicate with the auriculotemporal nerve distal to the TMJ.

In contrast to the innervation of the human TMJ, the facial nerve of the goat communicates with the auriculotemporal nerve proximal to the articular branches. The functional implications of this topography are unclear. Some afferents from the TMJ may travel centrally in the facial nerve or afferents in the facial nerve travel in the auriculotemporal nerve.

Thilander (1961) reported that the auriculotemporal nerve is the major sensory nerve of the TMJ. The branches from the auriculotemporal nerve innervate the posterior, medial, and lateral aspect of the anterior capsule. These branches enter the inferior aspect of the capsule along the neck of the condyle. This observation is not in accord with Rudinger (1857) who reported that the articular branches of the auriculotemporal nerve passed between the condyle and the pars tympanica. However, a recent study (Loughner et al., 1990) confirms Thilander's report. In this laboratory, macroscopic dissections of the TMJ of the goat (unpublished) show a similar course of the auriculotemporal nerve and distribution of articular branches.

According to Hilton's Law (1879), nerves that innervate the muscles that move a particular joint also contribute to innervation of the joint. Surprisingly, that contribution is only about 30% of the total TMJ innervation (Thilander, 1961). Twigs from the masseteric nerve innervate parts of the anterior capsule and anterior aspect of the medial capsule. The posterior deep temporal nerve innervate the lateral anterior aspect of the capsule. The auriculotemporal nerve supplies the remaining 70% of the TMJ.

Thilander (1961) estimated that the human TMJ is innervated by an average of 1500 peripheral afferent fibers. The auriculotemporal nerve contributes two thirds of the total amount. The greatest number of the articular fibers have a diameter between 1 and 2 μm and probably terminate as free endings in the capsule, posterior attachment tissues and adventitia of blood vessels associated with the joint. Other afferent fibers, though fewer in number, and ranging from 6 to 11 μm, terminate in complex neural endings.

The posterior attachment tissues contain a rich plexus of nerve fibers from the auriculotemporal nerve. Hall et al., (1985) identified and quantified the types of nerve fibers in the posterior attachment tissues. The authors found that the majority of axons were unmyelinated. The lateral portion of the posterior attachment tissues contain significantly higher percentage of unmyelinated fibers. Other investigators (Weinmann and Sicher, 1951; Sicher, 1955) have reported abundant innervation in association with blood vessels in the loose connective tissue between the posteror border of the articular disc and the capsule.

A few nerve fibers have been observed in the synovial membrane of the human TMJ (Thilander, 1961; Ishibashi, 1966). Ishibashi, (1974) found free nerve endings and glomerular endings beneath the superficial cell layer of the synovial membrane located on the posterior aspect of the TMJ. Bernick (1962) described encapsulated end bulbs in the synovial folds in the TMJ of the rat. These observations appear to contradict those who believe that the synovial tissue serves no sensory function (Olson, 1969). Although the nerve endings in the synovial membrane have been reported to be closely associated with blood vessels (Hagen-Torn, 1882; Davis, 1945), unmyelinated nerve fibers have been described in the synovium separated from blood vessels (Kellgren and Samuel, 1950; Rossie, 1950). Kawamura et al. (1967) found Golgi-type endings in the synovial tissue layer of the TMJ of the cat but not in the synovial membrane itself. Whether the synovial membrane is innervated or not, the justapositon of afferent fibers allows sensibility in the territory of the synovium.

As reported by Thilander (1961), the articular disc contained no nerve endings. However, other investigators (Ishibashi, 1966; Schmid, 1969; Zimny and St. Onge, 1987) described articular nerves innervating the periphery of the disc in the human TMJ. Similar results were reported in the monkey (Keller and Moffet, 1968), in the rat (Bernick, 1962) and in the mouse (Frommer and Monroe, 1966). These studies are consistent with histological studies of fetal material. Kitamura (1974) reported that, in the 5th month in

utero, nerve fibers were observed in the disc; further development was accompanied by a reduction in disc innervation. Corroboration of the influence of growth on disc innervation came from Hromada (1960), who observed free nerve endings in the disc of various animals; at older ages such endings were limited to the periphery of the disc. By comparison, the nerve supply to the meniscus of the human knee remains unclear (For review see Zimny, 1988). The most recent study (Albright and Zimny, 1987) reports that free and complex nerve endings were observed in outer and middle one-third of the meniscus; whereas, no innervation was found in the inner one-third.

Innervation of the TMJ of the monkey and cat resemble that of the human joint (Franks, 1965; Keller and Moffett, 1968). Branches from the deep temporal and masseteric nerves supply the anterior capsule, and the articular branches of the auriculotemporal nerve supply the TMJ posteriorly. Preliminary macrodissection of the nerves innervating the TMJ of one goat was performed in this laboratory. The auriculotemporal nerve gave off three articular branches along the posterior aspect of the neck of the condyle. The articular branches ascended into the fatty and fibrous articular tissue. The termination of the temporal branch of the auriculotemporal nerve appeared in the facial skin inferior to the zygomatic arch. The masseteric nerve was observed to arise from the anterior trunk of the mandibular nerve, course lateral along the anterior border of the capsule of the TMJ and terminate in the superficial and deep masseter muscle. Twigs from the masseteric nerve appeared to enter the anteriorlateral aspect of the capsule.

Tissues surrounding articulations possess fewer types of receptors than muscle or cutaneous tissue. Thilander (1961) described four types of neural endings in the human TMJ: Ruffini-like receptors, modified Pacinian endings, Golgi tendon organs and free nerve endings. Ishibashi (1966) also reported the presence of free nerve endings and complex terminal expansions in the human TMJ. Keller and Moffett (1968) reported free and complex nerve endings in the TMJ of monkeys. Many investigators have identified

free and complex nerve endings in the TMJ of the cat (Kawamura and Majima, 1964; Greenfield and Wyke, 1966; Kawamura et al., 1967; Wyke, 1967; Klineberg, 1971).

The three types of complicated nerve endings were sparsely distributed compared to the free nerve endings. The most common complex ending is the Ruffini ending. Ruffini-like endings were encountered in the lateral and posteriorlateral aspect of the capsule in humans (Thilander, 1961). Griffin and Harris (1975) described a thinly unencapsulated corpuscle located close to the periosteum of the neck of the condyle and in the lateral and medial aspects of the capsule fat pads. These receptors may have been similar to the Ruffini endings described by Klineberg (1971) in the TMJ of the cat. The Ruffini-type, low theshold mechanoreceptors were once thought to signal joint position (Boyd and Roberts, 1953; Boyd, 1954; Cohen, 1955; Skoglund, 1956, 1973). However, other investigators (Burgess and Clark, 1969; McCall et al., 1974; Clark and Burgess, 1975; Clark, 1975; Grigg, 1975; Grigg and Greenspan, 1977) have shown that Ruffini endings are seldom active at intermediate positions of the cat knee joint. They are responsive to extremes of joint movement. Consequently, these receptors are unlikely the peripheral neural substrate that code for position sense. Instead, Ruffini endings appear to signal the torque produced when the joint is extended and/or rotated at the limit of the range of motion. (Grigg et al., 1982a).

Pacinian endings were found in the lateral aspect of the capsule (Thilander, 1961). Paciniform-type end organs in cats have a similar distribution as Ruffini endings but less dense (Kawamura et al., 1967; Klineberg, 1971). Golgi tendon organs were located in the temporomandibular ligament and anterior capsule (Thilander, 1961; Griffin et al., 1965). In the anterior capsule, the Golgi end organ was in series with the extrafusal fibers of the lateral pterygoid muscle and tendon fasciculi of the capsular tissue or the fibrous tissue of the pes menisci. In the temporomandibular ligament the Golgi end organ was thought to be in series with fibers of the deep masseter muscle. Both Paciniform endings and Golgi tendon organs are thought to respond like comparable endings found in cutaneous and

muscle tissue (Willis and Coggeshall, 1978). However, Grigg et al., (1982b) showed that in the cat knee, Golgi tendon organs responded to local pressure applied perpendicular to the capsule but not to tension applied parallel to the capsule.

Free nerve endings are the most abundant receptor in the capsule of the human TMJ. Presumably, free nerve endings derived from myelinated afferents subserve fast pain sensibility and nociceptive somatic reflexes; free nerve endings derived from unmyelinated nerve fibers may subserve slow pain sensibility or innervate vascular elements. Free ending receptor specializations have yet to be defined. In sympathectomized cats, sensory nonmedullated plexuses have been found in the inner layers of the fibrous capsule, adjacent synovial tissues and adventitia of blood vessels in the knee joint of cat (Samuel, 1952). Free endings have been described in the joint capsule, joint ligaments and periarticular fat pads (Greenfield and Wyke, 1966). Similar results have been reported by Freeman and Wyke (1967). Free endings characteristic of group III and IV afferents have been described in the Archilles tendon of the cat as well (Andres et al., 1980). Some of these free endings may be nociceptors.

Although there are great variations in the morphology of the TMJ between species, the innervation of the TMJ is quite similar (Kawamura, 1980). The distribution and appearance of receptors may vary with age and species (Polacek, 1966), but the types of receptors are consonant across species including human.

In summary, the mammalian TMJ contains four types of receptors (for review see Skoglund, 1973; Zimny, 1988). The Ruffini and Paciniform mechanoreceptors are innervated by medium-sized (A_B) myelinated fibers, the Golgi tendon organ by large (A_a) myelinated fibers and the free endings by fine myelinated and unmyelinated afferents.

APPENDIX D

CENTRAL REPRESENTATION OF TMJ AFFERENTS

The central distribution of TMJ afferents has been studied in the trigeminal nuclear complex. The main sensory nuclei and the dorsal part of the rostral spinal nucleus were found to contain neurons responsive to isolated condylar movement or pressure applied to the joint capsule of the cat (Kawamura aand Majima, 1964; Kawamura et al., 1967). The authors reported simple, qualitative findings describing three types of responses to ipsilateral condylar rotation (rapidly adapting, slowly adapting and on-off types) and two types of responses to mechanical stimulation (rapidly adapting and slowly adapting types). In addition, response patterns of neurons in the trigeminal motor nucleus were recorded during condylar movements or mechanical stimulation of the joint capsule. As with responses from the sensory nuclei, no quantification of activity was attempted. Procaine infiltration into the joint capsule abolished neural responses. Another qualitative study reported unit activity found in the trigeminal main sensory nucleus and nucleus oralis of the cat that responded to jaw rotation or pressure applied to the ipsilateral TMJ (Sessle and Greenwood, 1976). One of these units was antidromically activated from the thalamus. Other direct projections from the superficial layers of the medullary dorsal horn to the thalamus have been demonstrated anatomically (Craig and Burton, 1981) and electrophysiologically (Dostrovsky and Broton, 1985).

The caudal aspects of the trigeminal nucleus complex were found to contain neurons that are driven by electrical, mechanical, and algesic chemical stimuli applied to the TMJ (Broton and Sessle, 1988). Neurons in the subnucleus caudalis were first classified

on the basis of their responsiveness to mechanical stimulation to the skin: low-threshold mechanoreceptors (LTM), wide dynamic range (WDR) or nociceptive specified (NS). WDR and NS neurons responded maximally to algesic chemical and intense mechanical stimulation applied to the joint. TMJ stimulation consisted of local probing or extreme jaw opening. The majority of single units with TMJ input received convergent input from cutaneous afferents. Kojima (1990) also found convergence patterns of afferent input from the TMJ and muscle in the subnucleus caudalis. Most of the units tested were responsive to mechanical and thermal stimulation of both the TMJ and the masseter muscle.

Extensive convergence of cutaneous and muscle inputs on second-order neurons that respond to articular movement have been described in the cat knee (Schaible et al., 1986). In some neurons, maximal responses to joint movement occurred with forced extension, inward rotation or outward rotation. Other neurons were excited only by noxious movement. Joint movement was considered noxious if the movement was made forceably. No quantification of forces was attempted. This report compares favorably with the effects of TMJ stimulation in neurons in the medullary dorsal horn (Broton and Sessle, 1988), in that most second order neurons that respond to noxious joint simulation also receive convergent input from skin and/or muscle. Such central convergence may be important in explaining the tenderness of skin and/or muscles near the joint that are often observed clinically when the joint is painful.

Changes in responsiveness in spinal neurons have been investigated during the development of acute arthritis in the cat knee jont (Neugebauer and Schaible, 1990). All neurons tested with joint input showed enhanced responsiveness to joint flexion after induction of inflammation.

Other electrophysiological experiments performed in polyarthritic rats demonstrated nociceptive inputs from chronically inflamed joints to the ventrobasal thalmus (Guilbaud et al., 1980; Gautron and Guilbaud, 1982), intralaminar and medial thalamus (Kayser and Guilbaud, 1984; Dostrovsky and Guilbaud, 1990), and somatosensory cortex (Lamour et

al., 1983). One consistent feature of the neuronal reactivity seen in all of these studies is the increase responsiveness of central neurons to non-noxious stimulation of the inflamed joints. The central mechanisms which might contribute to changes in responsiveness of central neurons in arthritic rats is still in question. The alterations in discharge behavior seen in CNS neurons is likely due, in part, to the changes in responsiveness of joint receptors due to inflammatory processes.

APPENDIX E

TRIGEMINAL GANGLION

The trigeminal ganglion is situated near the apex of the petrous bone in the middle cranial fossa. It lies in Meckel's cave near the cavernous sinus and internal carotid artery. The sensory root (portio major) enters the pons in association with the motor root (portio minor), which courses dorsomedially, and terminates in the trigeminal nuclear complex.

Sensory input from the face enters the trigeminal ganglion via the opthalamic, maxillary and mandibular division of the trigeminal nerve. The cell bodies of these afferent fibers are segregated into discrete clusters (Jerge, 1964; Kerr, 1962).

Retrograph transport of HRP injected into the cat TMJ showed that sensory neurons originate in the trigeminal ganglion (Romfh et al., 1979; Capra, 1987). Whether all of the cell bodies of afferent neurons innervating the TMJ are located in the trigeminal ganglion remains unanswered. There is evidence suggesting that the peripheral spinal neurons innervate the TMJ. Widenfalk and Wiberg (1990) injected HRP into the TMJ of rats. Labeled cells were observed ipsilaterally in the second to fifth dorsal root ganglion. In addition, there is evidence suggesting that the mesencephalic nucleus contains cell bodies of neurons that terminate in the TMJ. In a preliminary communication, Limwongee (1986) reported injection of HRP into the TMJ of rat, cat and monkey. He found labeled neurons in the mesencephalic nucleus at the level of the caudal pons. On the other hand, Corbin (1940) ablated the mesencephalic nucleus and examined histologically the auriculotemporal nerve. He found no degenerated fibers. In addition, Chen and Turner (1987) injected

HRP into the TMJ and insertion of the lateral pterygoid muscle of rats. They found no central projection to the mesencephalic nucleus.

Somatotopy

There is general agreement that the trigeminal ganglion in cats is somatopically represented from a medial to lateral direction (Beaudreau and Jerge, 1968; Zucker and Welker, 1969; Kerr and Lysak, 1964; Darian-Smith et al., 1965; Marfurt, 1981). The ophthalmic division lies anteriomedially, the mandibular division lies posteriolaterally and the maxillary division is situated in an intermediate position. Overlap between divisions has been reported (Marfurt, 1981; Henry et al., 1986). Romfh et al., (1979) and Capra (1987) reported that injection of HRP into the capsular tissues of the TMJ in the cat resulted in a restricted distribution of label in the posteriolateral position of the trigeminal ganglion. Very few labeled cells were found in the most dorsal or in the most ventral areas of the mandibular division of the trigeminal ganglion. The majority of labeled cells is found throughout the intermediate zone in the posteriolateral part of the ganglion. Electrophysiological studies in cats (Capra and Gaitpon, 1981) and in rabbits (Lund and Matthews, 1981; Appenteng et al., 1982) confirmed that TMJ afferents were located in the posteriolateral region of the trigeminal ganglion.

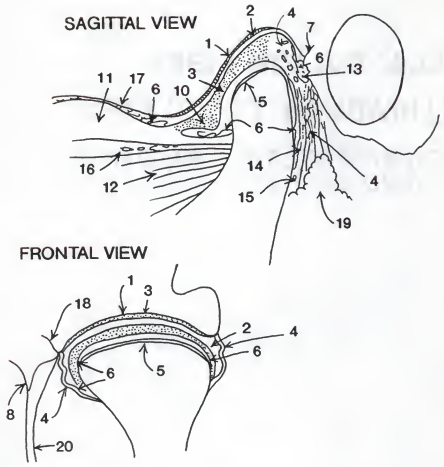
In addition to the mediolateral somatotopy , studies suggest a dorsoventral somatotopic organization (Kerr and Lysak, 1964; Marfurt, 1981; Capra, 1987). Representation of oral and perioral structures appear ventral in the ganglion. Areas remote from the mouth lie in the dorsum of the ganglion.

APPENDIX F

GROSS ANATOMY

The TMJ in mammals is a ginglymus-arthroidal joint, i.e., a hinge joint capable of gliding movement (Figure F-1). The craniomandibular articulation involves the condyle of the mandible juxtaposed with the articular surface of the squamous portion of the temporal bone. Interposed between the condyle and the articular fossa is an articular disk dividing the articular space into upper and lower compartments.

The periarticular soft tissue consists of fibrous capsule, posterior attachment tissues, synovial membrane and accessory ligaments. Except for the synovial membrane, these tissues serve to limit the range of motion of the joint and to maintain a packed position (Sicher, 1960; Rocabado, 1983). A packed position is the condyle-disc-fossa relationship which juxtaposes these TMJ elements at rest and during mandibular movements. The joint capsule is loose and composed of dense connective tissue with a collagenous matrix richly supplied with blood vessels and nerves. The dense connective tissue of the capsule is located primarily on the lateral and medial aspect of the joint and intimately associated with the temporomandibular and sphenomandibular ligaments, respectively. The anterior capsule arises from the suture line between the greater wing of the sphenoid bone and the temporal bone. It inserts on the anteriorlateral aspect of the condylar neck. The loose connective tissue of the capsule encompasses the joint posteriorly. It arises from the tragal cartilage laterally and tympanic plate medially. The posterior capsule, as a meshwork of unorganized collagen fiber, inserts and blends in with the posterior periosteum of the condylar neck and upper capsule of the parotid gland.



1. Articular Surface of Glenoid Fossa
2. Superior Cavitt
3. Disc (Stippled Area)
4. Capsule
5. Articular Surface of Condyle
6. Synovial Membrane
7. Squamo-Tympanic Suture
8. Spine of the Sphenoid
9. Vascular Knee of Meniscus
10. Pes Meniscus
11. Superior Belly of Lat. Pterygoid
12. Inferior Belly of Lat. Pterygoid
13. Superior Stratum of Bilaminar Zone of Meniscus
14. Inferior Stratum of Bilaminar Zone of Meniscus
15. Auriculotemporal Nerve
16. Blood Vessels
17. Posterior Deep Temporal Nerve
18. Squamo-Sphenoidal Suture
19. Parotid Gland
20. Sphenomandibular Ligament

Figure F-1

Schematic diagram of the human temporomandibular joint. Sagittal and frontal views.

The dense connective tissue of the capsule reinforces the lateral position of the TMJ and is incorporated into the temporomandibular ligament. Horizontal fibers of the temporomandibular ligament restrict posterior displacement of the condyle and oblique fibers tend to limit lateral and inferior displacement (Sicher, 1960; Griffin and Malor, 1974). The posterior attachment tissues consists of collagenous and elastic connective tissues which extend from the posterior border of the disc to the tympanic plate.

Macroscopic dissections of the goat TMJ were performed in this laboratory. The articular surface of the condyle is oval in shape, its longer dimension is concave mediolateral and the shorter dimension is convex anterioposterior. The articular disc is ovoid, biconcave, and divides the joint into two synovial cavities. The fibrous capsule is moderately loose which allows for extensive lateral translation of the condyle. The capsule surrounds the joint, with the exception of the anteriomedial portions, where the lateral pterygoid muscle attaches to the neck of the condyle. With four exceptions the gross anatomy of the goat TMJ is similar to the human. First, the lateral aspect of the posterior attachment tissue extends posteriorly beyond the postglenoid process and attaches to the inferior surface of the zygomatic process of the temporal bone. This anatomical variation is associated with the lateralization of the bony articulation of the TMJ beyond the cranial base. Second, the articular surface of the glenoid fossa is slightly convex in all directions, rather than concave. To accommodate this convexity the condyle is appropriately concave along the mediallateral axis. Third, there is no articular eminence. Finally, the lateral pterygoid muscle attaches to the anteriormedial aspect of the neck of the condyle in a manner similar to the human, but it does not appear to attach to the disc.

Comparative Anatomy

According to the classification of Turnbull (1970), goats are section II herbivors while humans are section III omnivores. The TMJ of the goat has been used as an animal

model for oral surgery procedures because the anatomy and biomechanics are similar to the human TMJ (Bifano et al., 1990).

First, for the vertebrate chewing apparatus, the range of motion is generally confined to those movements necessary for dealing with a particular diet. Due to a coarse diet of vegetation, ruminants possess a greater range of mandibular movement than do carnivores. The excursive movements include hinging, lateral translation, slight protrusion and mediolateral shift. Hinge opening and lateral translational movements are required for forceful grinding. The lateral pterygoid muscle is the prime mover of the mandible during lateral translational movements. The lateral excursion, initiated by contraction of either one of the lateral pterygoid muscles, is a prerequisite to an effective grinding stroke. Both the goat and human possess a well-developed, lateral pterygoid muscle.

Second, the elevated position of the condyle of the mandible relative to the occlusal plane benefits the operation of the masseter and medial pterygoid muscles. They function synergistically to provide powerful bite force needed for grinding activity.

Third, the condyle is convex anteriorposteriorly, which allows some translation along a convex articular surface of the fossa. Such anteriorposterior translation represents a common denominator between the TMJ of non-carnivorous mammals and the human joints. In contrast, carnivores have a deep concave articular fossa that allows only hinge movement and prevents dislocation during seizure of prey.

APPENDIX G

SUMMARY TABLES OF TMJ REACTIVITY

TABLE G-1
REACTIVITY IN VERTICAL PLANE
NORMAL TISSUE

	FILE		FUNCTION	TEST	FREQ. THRES	ACT. THRES	FREQ. ASYM.	MRI	R^2	RF (gr)	CV (m/sec)
1	021691E	E3	LnI = -1.2LnF + 7.6	DF	.	14N	30N	4.3	0.56	3.6	0.7
1	021691E	E3	LnI = -1.4LnF + 8.4	M	.	14°	26°	4.9	0.59	3.6	0.7
2	040690S	S3	LnI = -3.4LnF + 11.2	DF	.	15N	19N	6.5	0.25	28.0	0.4
2	040690S	S3	LnI = -0.37LnF + 2.9	FV	.	6 N/s	91N/s	1.3	0.26	28.0	0.4
2	040690S!	S3	LnI = -1.8LnF + 5.5	M	.	7°	10°	3.5	0.20	28.0	0.4
2	040690T	T3	LnI = -5.0LnF + 1.0	SF	7.0N	9N	15N	6.0	0.73	28.0	0.4
2	040690T!	T3	LnI = -5.8 LnF + 17.0	P	10°	10°	16°	6.6	0.73	28.0	0.4
3	041390K	K7	LnI = -1.1LnF + 5.5	DF	.	13N	31N	2.3	0.10	5.4	.
3	041390N	N7	LnI = -0.6LnF + 4.8	FV	.	2N/s	90N/s	2.1	0.10	5.4	.
4	042090H	H6	LnI = -3.0LnF + 16.0	DF	.	41N	62N	6.9	0.64	76.0	.
4	042090H!	H6	LnI = -5.0LnF + 16.0	M	.	8°	10°	13.0	0.64	76.0	.
5	102690D	D1	LnI = -0.8LnF + 7.0	DF	.	32N	122N	3.4	0.29	5.4	.
5	102690D	D1	LnI = -0.6LnF + 6.4	FV	.	42N/s	218N/s	3.3	0.30	5.4	.
6	110990E	E2	LnI = -2.7LnF + 11.0	DF	.	20N	24N	7.3	0.53	3.6	.
6	110990E	E2	LnI = -1.1LnF + 7.7	FV	.	45N/s	129N/s	2.8	0.76	3.6	.
6	110990D	D2	LnI = -0.9LnF + 7.0	SF	8.0N	30N	65N	3.8	0.66	3.6	.
6	110990E!	E2	LnI = -6.6LnF + 19.0	M	.	10°	12°	14.0	0.73	3.6	.
7	111490E	E2	LnI = -1.3LnF + 8.1	DF	.	30N	88N	2.8	0.54	29.0	.
7	111490E	E2	LnI = -0.3LnF + 4.6	FV	.	29N/s	296N/s	2.9	0.25	29.0	.
7	111490F	F2	LnI = -0.44LnF + 5.7	SF	27N	58N	96N	4.1	0.86	20.0	.
8	111490L	L3	LnI = -1.1LnF + 7.5	DF	.	25N	77N	3.2	0.73	5.4	.
8	111490L	L3	LnI = -0.22LnF + 4.0	FV	.	11N/s	142N/s	2.9	0.20	5.4	.
8	111490J!	J3	LnI = -6.2LnF + 21.0	M	.	15°	22°	9.0	0.31	5.4	.
9	121490A	A1	LnI = -1.3LnF + 9.6	DF	.	38N	113N	4.0	0.68	12.5	.
10	030791A	A1	LnI = -0.9LnF + 7.2	FV	.	10N/s	48N/s	6.3	0.50	5.4	.
11	032091G	G3	LnI = -0.7LnF + 6.5	DF	.	12N	36N	4.3	0.40	5.4	7.5
11	032091G	G3	LnI = -0.17LnF + 4.8	FV	.	6N/s	170N/s	3.9	0.19	5.4	7.5

TABLE G-2

REACTIVITY IN HORIZONTAL PLANE

NORMAL TISSUE

LEFT LATERAL

	FILE		FUNCTION	TEST	FREQ. THRES	ACT. THRES	FREQ. ASYM.	MRI	R^2	RF (gr)	CV (m/sec)
1	021690A	A1	LnI = -1.4LnF + 5.1	SF	3.0N	3.0N	30N	0.5	0.93	8.5	.
2	110990A	A1	LnI = -0.4LnF + 5.0	DF	.	30N	100N	3.3	0.10	15.0	.
3	121990A	A1	LnI = -1.0LnF + 5.0	DF	.	6.0N	15N	2.8	0.27	8.5	.
3	121990A	A1	LnI = -0.3LnF + 3.4	FV	.	1.0N/s	35N/s	2.3	0.32	8.5	.
4	011691A	A1	LnI = -0.7LnF + 4.8	DF	.	8.0N	33N	2.6	0.40	5.5	2.5
4	011691A	A1	LnI = -0.2LnF + 3.8	FV	.	25N/s	267N/s	2.7	0.17	5.5	2.5
4	011691B	B1	LnI = -1.8LnF + 8.7	SF	6.0N	16N	42N	2.8	0.97	5.5	2.5
5	011691C	C2	LnI = -0.7LnF + 4.8	DF	.	6.0N	34N	2.4	0.77	76.0	.
5	011691C	C2	LnI = -0.34LnF + 4.4	FV	.	62N/s	305N/s	2.5	0.34	76.0	.
5	011691D	D2	LnI = -1.2LnF + 6.3	SF	4.5N	10N	19N	3.7	0.95	76.0	.
6	012391A	A2	LnI = -0.5LnF + 4.7	DF	.	9.5N	56N	2.8	0.31	29.0	.
6	012391A	A2	LnI = -0.1LnF + 3.4	FV	.	7.0N/s	119N/s	2.9	0.10	29.0	.
7	022091A	A1	LnI = -1.3LnF + 7.0	DF	.	7.0N	31N	2.9	0.75	15.0	.
7	022091A	A1	LnI = -0.3LnF + 4.7	FV	.	2.0N/s	134N/s	3.2	0.50	15.0	.
7	022091B	B1	LnI = -1.4LnF + 8.4	SF	6.0N	12N	38N	3.8	0.64	15.0	.
8	031391A	A1	LnI = -3.0LnF + 14.0	DF	.	18N	34N	3.4	0.73	3.6	.
9	031391D	D3	LnI = -0.42LnF + 5.7	DF	.	5.0N	43N	4.2	0.23	5.5	.
9	031391D	D3	LnI = -0.16LnF + 4.9	FV	.	6.0N/s	171N/s	4.1	0.16	5.5	.
10	032091D	D2	LnI = -0.38LnF + 4.6	DF	.	5.0N	20N	3.6	0.17	3.6	.
10	032091E	E2	LnI = -0.36LnF + 5.0	SF	2.0N	4.0N	35N	3.8	0.28	3.6	.
11	032891J	J4	LnI = -0.8LnF + 6.9	DF	.	10N	25N	4.7	0.32	5.5	.
11	032891J	J4	LnI = -0.2LnF + 5.0	FV	.	6.0N/s	133N/s	4.0	0.29	5.5	.
12	042491A	A1	LnI = -0.7LnF + 5.3	DF	.	6.0N	19N	3.5	0.60	29.0	.
13	072691A	A1	LnI = -0.78LnF + 5.5	DF	.	13N	40N	2.9	0.19	5.5	.
14	092791H	H	LnI = -0.49LnF + 3.9	DF	.	3.0N	31N	2.3	0.27	3.6	.

TABLE G-3

REACTIVITY IN HORIZONTAL PLANE

NORMAL TISSUE

RIGHT LATERAL

	FILE		FUNCTION	TEST	FREQ. THRES	ACT. THRES	FREQ. ASYM	MRI	R^2	RF (gr)	CV (msec)
1	031391B	B2	LnI = -0.59LnF + 5.3	DF	.	8.0N	19N	3.9	0.33	5.5	.
2	041091A	A2	LnI = -2.1LnF + 8.3	DF	.	9.0N	12N	6.0	0.91	5.5	.
3	042491G2	G3	LnI = -2.2LnF +10.4	SF	12N	14N	26N	5.0	0.38	5.5	.
4	042491I	I4	LnI = -2.0LnF + 7.8	DF	.	4.0N	17N	2.7	0.70	5.5	.
4	042491I	I4	LnI = -0.3LnF + 3.4	FV	.	2.0N	50N/s	2.2	0.26	5.5	.
4	042491J	I4	LnI = -4.0LnF +13.0	SF	5.0N	9.0N	14N	6.6	0.97	5.5	.

TABLE G-4
REACTIVITY IN THE VERTICAL PLANE
IN PREVIOUSLY INFLAMED TISSUE

	FILE		FUNCTION	TEST	FREQ. THRES.	ACT. THRES.	FREQ. ASYM	R^2	MRI (m/sec)	RF (gr)	CV (m/sec)
1	021089B2	B2	LnI = -0.29LnF+ 3.3	FV	.	9.0N/s	60N/s	0.11	2.2	15.0	.
2	021089T	T7	LnI = -0.49LnF+ 3.0	DF	.	1.0N	4.0N	0.10	2.5	15.0	.
2	021089T	T7	LnI = -0.5LnF + 3.3	FV	.	0.8N/s	26N/s	0.26	2.7	15.0	.
3	021089EE	E11	LnI = -1.6LnF + 2.5	DF	.	0.35N	1.0N	0.19	3.2	15.0	.
3	021089EE	E11	LnI = -2.4LnF + 3.2	FV	.	0.4N/s	3.3N/s	0.85	0.6	15.0	.
4	021089JJ	J13	LnI = -1.8LnF + 5.4	DF	.	4.0N	8.0N	0.11	2.9	15.0	.
4	021089JJ	J13	LnI = -0.5LnF + 3.2	FV	.	0.8N/s	58N/s	0.41	1.2	15.0	.
5	041091E	E3	LnI = -1.1LnF + 9.1	DF	.	28N	67N	0.50	5.1	5.0	.
5	041091E	E3	LnI = -0.26LnF+ 5.2	FV	.	10N/s	40N/s	0.20	4.3	5.0	.
5	041091E!	E3	LnI = -6.6LnM + 24.0	M	.	17°	20°	0.46	17.0	5.0	.
5	041091F	F3	LnI = -0.68LnF+ 6.3	SF	3.0N	4.0N	19N	0.44	4.5	5.0	.
5	041091F!	F3	LnI = -2.0 LnP + 10.0	P	7°	10°	17°	0.42	6.1	5.0	.

REACTIVITY IN HORIZONTAL PLANE
IN PREVIOUSLY INFLAMED TISSUE
LEFT LATERAL

	FILE		FUNCTION	TEST	FREQ. THRES.	ACT. THRES.	FREQ. ASYM.	R^2	MRI (m/sec)	RF (gr)	CV (m/sec)
1	033090T	T15	LnI = -0.2 LnF + 3.0	FV	.	7.5N/s	54N/s	2.2	0.12	125.0	0.67
1	033090U	U15	LnI =-1.9LnF + 9.6	SF	9.1N	9.1N	32N	3.7	0.28	125.0	0.67
1	033090TS	T15	LnI = -0.84LnF+ 6.6	DF	.	19N	55N	3.6	0.20	125.0	0.67
2	0509910	O2	LnI = -0.59LnF+ 5.9	DF	.	18N	65N	3.6	0.36	5.5	.

TABLE G-5
TMJ NOCICEPTOR REACTIVITY IN NORMAL TISSUE
VERTICAL PLANE

Test Conditions	with RF (n=18)		without RF (n-9)	
	code (n=11)	no code (n=7)	code (n=8)	no code (n=1)
Dynamic Force	10	8	6	3
Force Velocity	8	10	4	5
Movement	5	10	2	3
Static Force	3	12	1	4
Position	1	14	0	4
Conduction Velocity	0.4 to 7.5 m/sec (n=4)	0.75 to 1.5 m/sec (n=2)	.	.
Post-test Spontaneous Activity	2	0	0	0

TABLE G-6
TMJ NOCICEPTOR REACTIVITY IN NORMAL TISSUE
HORIZONTAL PLANE

Test Conditions	with RF (n=18)		without RF (n-9)	
	code (n=14)	no code (n=3)	code (n=1)	no code (n=4)
Dynamic Force	13	4	0	3
Force Velocity	7	9	0	3
Static Force	5	11	0	0
Conduction Velocity	2.5 to 3.3 m/sec (n=2)	0.5 m/sec (n=1)	.	.
Post-test Spontaneous Activity	1	0	0	0

TABLE G-7
TMJ NOCICEPTOR REACTIVITY
IN PREVIOUSLY INFLAMED TISSUE

Test Conditions	with RF (n=7)		without RF (n-8)	
	code (n=7)	no code (n=0)	code (n=6)	no code (n=2)
Dynamic Force	6	0	4	2
Force Velocity	6	0	5	2
Movement	1	0	0	0
Static Force	2	0	0	0
Position	1	0	0	0
Conduction Velocity	0.7m/sec (n=1)	0	0	0
Post-test Spontaneous Activity	0	0	0	0

TABLE G-8
TMJ NOCICEPTOR REACTIVITY
IN ACUTELY INFLAMED TISSUE

Test Conditions	with RF (n=11)	
	code (n=9)	acquired coding (n=8)
Dynamic Force	9	2
Force Velocity	4	4
Movement	2	0
Static Force	4	5
Position	1	1
Conduction Velocity	0.8 to 6.0 m/sec (n=6)	.
Post-test Spontaneous Activity	.	6

TABLE G-9
TMJ NOCICEPTOR REACTIVITY
IN SALINE INJECTED TISSUE

Test Conditions	with RF (n=8)	
	code (n=7)	acquired coding (n=1)
Dynamic Force	6	0
Force Velocity	2	1
Movement	0	0
Static Force	6	0
Position	0	0
Conduction Velocity	0.5-8.5 m/sec (n=2)	.
Post-test Spontaneous Activity	.	0

TABLE G-10

EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE REACTIVITY IN THE VERTICAL PLANE
UNIT #1

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	12N	1.7N	-10.3N
	Freq. Asymptote	50N	69N	19N
	Mean Rate	3.4	2.7	-0.7
	Slope	-0.44	-0.19	-0.25
	Freq. Thres.	.	.	.
	R^2	0.18	0.44	0.26
Static Force	Act. Thres.	7N	1.6	-5.4N
	Freq. Asymptote	17N	30N	13N
	Mean Rate	4.5	5.1	0.6
	Slope	-0.4	-0.68	-0.28
	Freq. Thres.	10N	1.6N	-8.4N
	R^2	0.23	0.60	0.42
Position	Act. Thres.	10.5°	3.4°	-7.1°
	Freq. Asymptote	16°	22°	6.0°
	Mean Rate	5.2	3.3	-1.5
	Slope	-1.1	-1.2	-0.1
	Freq. Thres.	10.0	2.7°	-7.3°
	R^2	0.35	0.79	0.44
Movement	Act. Thres.	9.8°	6.2°	-3.6°
	Freq. Asymptote	14°	25°	11°
	Mean Rate	7.3	3.13	-4.13
	Slope	-4.0	-0.5	3.5
	Freq Thres.	.	.	.
	R^2	0.6	0.47	-0.13
Force Velocity	Act. Thres.	.	2.0 N/s	.
	Freq. Asymptote	.	317 N/s	.
	Mean Rate	.	2.8	.
	Slope	.	-0.11	.
	Freq Thres.	.	.	.
	R^2	.	0.35	.

TABLE G-11
EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE
REACTIVITY IN THE VERTICAL PLANE
UNIT #2

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	6.0N	27N	21N
	Freq. Asymptote	33N	66N	33N
	Mean Rate	4.8	3.0	-1.8
	Slope	-0.44	-0.46	0.01
	Freq. Thres.	.	.	.
	R^2	0.42	0.11	-0.31
Movement	Act. Thres.	8.0°	23°	15°
	Freq. Asymptote	24°	28°	4.0°
	Mean Rate	4.1	7.3	3.2
	Slope	-0.8	-2.5	1.7
	Freq. Thres.	.	.	.
	R^2	0.48	0.19	-0.29
Static Force	Act. Thres.	.	25N	.
	Freq. Asymptote	.	59N	.
	Mean Rate	.	3.6	.
	Slope	.	-1.5	.
	Freq Thres.	.	12.0	.
	R^2	.	0.62	.

TABLE G-12
EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE REACTIVITY IN THE VERTICAL PLANE
UNIT #3

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	26N	40.7N	14.7N
	Freq. Asymptote	50N	76N	26N
	Mean Rate	4.4	2.8	-1.6
	Slope	-2.7	-1.17	-1.5
	Freq. Thres.	.	.	.
	R^2	0.50	0.10	-0.40
Movement	Act. Thres.	21°	24°	3.0°
	Freq. Asymptote	26°	25.5°	-0.5°
	Mean Rate	14	22	8.0
	Slope	-7.0	-7.9	0.9
	Freq. Thres.	24°	26°	20°
	R^2	0.40	0.90	0.50
Force Velocity	Act. Thres.	.	20.0N/s	.
	Freq. Asymptote	.	285N/s	.
	Mean Rate	.	1.9	.
	Slope	.	-0.4	.
	Freq Thres.	.	.	.
	R^2	.	0.13	.

TABLE G-13
EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE
REACTIVITY IN THE VERTICAL PLANE
UNIT #4

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	17N	49N	32N
	Freq. Asymptote	7.5N	23N	15.5N
	Mean Rate	3.8	3.7	-1.1
	Slope	-0.6	-1.0	0.4
	Freq. Thres.	.	.	.
	R^2	0.33	0.52	0.19
Movement	Act. Thres.	18°	11°	-7.0°
	Freq. Asymptote	29°	20°	-9.0°
	Mean Rate	5.3	4.2	-1.1
	Slope	-2.1	-1.7	-0.4
	Freq. Thres.	.	.	.
	R^2	0.32	0.66	0.34
Position	Act. Thres.	.	20°	.
	Freq. Asymptote	.	29°	.
	Mean Rate	.	7.7	.
	Slope	.	-3.3	.
	Freq. Thres.	.	-14.7°	.
	R^2	.	0.65	.
Force Velocity	Act. Thres.	2.2N/s	.	.
	Freq. Asymptote	23.5N/s	.	.
	Mean Rate	3.2	.	.
	Slope	-0.12	.	.
	Freq Thres.	.	.	.
	R^2	0.11	.	.

TABLE G-14

EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE REACTIVITY IN THE HORIZONTAL PLANE

UNIT #1

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	.	1.4N	.
	Freq. Asymptote	.	34N	.
	Mean Rate	.	4.1	.
	Slope	.	-0.6	.
	Freq. Thres.	.	.	.
	R^2	.	0.45	.
Force Velocity	Act. Thres.	.	3.0N/s	.
	Freq. Asymptote	.	132N/s	.
	Mean Rate	.	3.9	.
	Slope	.	-0.08	.
	Freq. Thres.	.		.
	R^2	.	0.12	.
Static Force	Act. Thres.	.	10.7N	.
	Freq. Asymptote	.	29N	.
	Mean Rate	.	4.6	.
	Slope	.	-0.97	.
	Freq Thres.	.	2.8N	.
	R^2	.	0.37	.

TABLE G-15
EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #2

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	2.7N	1.3N	-1.4N
	Freq. Asymptote	30N	32N	2.0N
	Mean Rate	2.0	3.4	0.5
	Slope	-1.1	-0.5	-0.6
	Freq. Thres.	.	.	.
	R^2	0.63	0.49	-0.14
Force Velocity	Act. Thres.	1N/s	1.6N/s	0.6N/s
	Freq. Asymptote	286N/s	185N/s	-101N/s
	Mean Rate	2.5	3.5	1.0
	Slope	-0.26	-0.17	-0.09
	Freq. Thres.	.	.	.
	R^2	0.30	0.29	-0.01
Static Force	Act. Thres.	.	3.2N	.
	Freq. Asymptote	.	30N	.
	Mean Rate	.	4.2	.
	Slope	.	-0.6	.
	Freq Thres.	.	2.1N	.
	R^2	.	0.63	.

TABLE G-16

EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE REACTIVITY IN THE HORIZONTAL PLANE
UNIT #3

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	3.0N	6.3N	3.3N
	Freq. Asymptote	33N	13N	-20N
	Mean Rate	2.9	4.0	1.1
	Slope	-0.58	-1.0	1.32
	Freq. Thres.	.	.	.
	R^2	0.53	0.64	0.11
Force Velocity	Act. Thres.	1N/s	13N/s	12N/s
	Freq. Asymptote	171N/s	179N/s	8N/s
	Mean Rate	3.1	2.9	-0.2
	Slope	-0.18	-1.2	1.38
	Freq. Thres.	.	.	.
	R^2	0.38	0.69	0.31
Static Force	Act. Thres.	.	3.9N	.
	Freq. Asymptote	.	7.9N	.
	Mean Rate	.	4.7	.
	Slope	.	-2.0	.
	Freq Thres.	.	2.9N	.
	R^2	.	0.60	.

TABLE G-17
EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #4

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	9.5N	6.4N	-3.1N
	Freq. Asymptote	52N	50N	-2.0N
	Mean Rate	3.2	3.4	0.2
	Slope	-0.27	-0.7	0.43
	Freq. Thres.	.	.	.
	R^2	0.11	0.60	0.49
Force Velocity	Act. Thres.	27N/s	5.0N/s	-22N/s
	Freq. Asymptote	333N/s	155N/s	-178N/s
	Mean Rate	2.9	3.1	-0.2
	Slope	-0.34	-0.25	-0.09
	Freq. Thres.	.	.	.
	R^2	0.39	0.26	-0.13
Static Force	Act. Thres.	19N	18N	-1.0N
	Freq. Asymptote	41N	52N	11N
	Mean Rate	4.2	3.7	-0.5
	Slope	-1.04	-1.5	0.46
	Freq Thres.	10.7N	9.0N	-1.7N
	R^2	0.50	0.70	0.20

TABLE G-18
EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #5

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	13.6N	1.4N	-12.2N
	Freq. Asymptote	17.9N	8.8N	-9.1N
	Mean Rate	4.7	2.5	-2.2
	Slope	-4.3	-1.5	-2.8
	Freq. Thres.	.	.	.
	R^2	0.84	0.28	-0.56

TABLE G-19
EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #6

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	27N	10N	-17N
	Freq. Asymptote	58N	34N	-24N
	Mean Rate	3.5	2.9	-0.6
	Slope	-0.88	-0.34	0.54
	Freq. Thres.	.	.	.
	R^2	0.30	0.28	-0.02
Static Force	Act. Thres.	35N	6.0N	-29N
	Freq. Asymptote	41N	48N	7.0N
	Mean Rate	7.9	4.6	-3.3
	Slope	-1.5	-0.3	-1.2
	Freq. Thres.	4.0N	5.0N	1.0N
	R^2	0.90	0.38	-0.52

TABLE G-20

EFFECT OF CARRAGEENAN IN ACUTELY INFLAMED TISSUE REACTIVITY IN THE HORIZONTAL PLANE

UNIT #7

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	.	7.9N	.
	Freq. Asymptote	.	30N	.
	Mean Rate	.	4.8	.
	Slope	.	-1.04	.
	Freq. Thres.	.	.	.
	R^2	.	0.58	.
Movement	Act. Thres.	.	1.0N/s	.
	Freq. Asymptote	.	40N/s	.
	Mean Rate	.	4.6	.
	Slope	.	-0.32	.
	Freq. Thres.	.	.	.
	R^2	.	0.40	.
Force Velocity	Act. Thres.	.	3.1N	.
	Freq. Asymptote	.	4.3N	.
	Mean Rate	.	8.3	.
	Slope	.	-2.7	.
	Freq Thres.	.	3.1N	.
	R^2	.	0.47	.

TABLE G-21

EFFECT OF SALINE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #1

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	4.3N	6.4N	2.1N
	Freq. Asymptote	26N	35N	9.0N
	Mean Rate	2.5	3.2	0.7
	Slope	-2.1	-0.74	-1.36
	Freq. Thres.	.	.	.
	R^2	0.77	0.27	-0.50
Force Velocity	Act. Thres.	7.0N	5.0N/s	-2.0N
	Freq. Asymptote	122N	154N/s	13N/s
	Mean Rate	2.0	2.6	0.6
	Slope	-0.57	-0.21	-0.36
	Freq. Thres.	.	.	.
	R^2	0.42	0.31	-0.11
Static Force	Act. Thres.	7.1N	2.8N	-4.3N
	Freq. Asymptote	27N	29N	2.0N
	Mean Rate	2.9	2.9	0.0
	Slope	-1.5	-.72	-0.78
	Freq Thres.	7.0N	1.4N	-5.6N
	R^2	0.60	0.68	0.08

TABLE G-22

EFFECT OF SALINE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #2

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	6.9N	7.0N	0.1N
	Freq. Asymptote	48N	46	-2.0N
	Mean Rate	3.6	3.5	- 0.1
	Slope	-0.35	-0.62	0.27
	Freq. Thres.	.	.	.
	R^2	0.20	0.59	0.39
Static Force	Act. Thres.	20N	11N	-9.0N
	Freq. Asymptote	49N	60N	11N
	Mean Rate	4.0	3.1	-0.9
	Slope	-1.4	-0.99	-0.42
	Freq. Thres.	.	9.0N	-5.0N
	R^2	0.66	0.52	-0.14
Force Velocity	Act. Thres.	.	13N/s	.
	Freq. Asymptote	.	179N/9	.
	Mean Rate	.	3.3	.
	Slope	.	-0.4	.
	Freq Thres.	.	.	.
	R^2	.	0.63	.

TABLE G-23

EFFECT OF SALINE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #3

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	13N	15N	2.0N
	Freq. Asymptote	49N	28N	-21N
	Mean Rate	3.5	3.5	0.0
	Slope	-0.74	-0.83	0.09
	Freq. Thres.	.	.	.
	R^2	0.45	0.28	-0.11
Static Force	Act. Thres.	11N	7.0N	-4.0N
	Freq. Asymptote	38N	41N	3.0N
	Mean Rate	3.75	3.71	-0.04
	Slope	-0.53	-0.48	-0.05
	Freq. Thres.	8.0N	6.0N	-2.0N
	R^2	0.36	0.28	-0.08

TABLE G-24

EFFECT OF SALINE
REACTIVITY IN THE VERTICAL PLANE
UNIT #4

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	5.7N	.	.
	Freq. Asymptote	54N	.	.
	Mean Rate	3.2	.	.
	Slope	-0.55	.	.
	Freq. Thres.	.	.	.
	R^2	0.53	.	.
Force Velocity	Act. Thres.	11N	.	.
	Freq. Asymptote	257N	.	.
	Mean Rate	3.1	.	.
	Slope	-0.3	.	.
	Freq. Thres.	.	.	.
	R^2	0.51	.	.
Movement	Act. Thres.	9.9°	.	.
	Freq. Asymptote	25°	.	.
	Mean Rate	3.9	.	.
	Slope	-1.5	.	.
	Freq. Thres.	.	.	.
	R^2	0.58	.	.
Static Force	Act. Thres.	6.4N	.	.
	Freq. Asymptote	50N	.	.
	Mean Rate	3.4	.	.
	Slope	-0.8	.	.
	Freq Thres.	3.0N	.	.
	R^2	0.65		.
Position	Act. Thres.	15°	.	.
	Freq. Asymptote	25°	.	.
	Mean Rate	5.6	.	.
	Slope	-0.32	.	.
	Freq Thres.	9.0°	.	.
	R^2	0.62	.	.

TABLE G-25

EFFECT OF SALINE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #6

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	46N	25N	-21N
	Freq. Asymptote	71N	59N	-12N
	Mean Rate	5.5	4.2	-1.3
	Slope	-1.7	-1.2	-0.05
	Freq. Thres.	.	.	.
	R^2	0.37	0.43	-0.06

TABLE G-26
EFFECT OF SALINE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #7

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	7.4N	11N	3.6N
	Freq. Asymptote	59N	68N	9.0N
	Mean Rate	3.6	3.8	0.2
	Slope	-0.54	-0.27	-0.27
	Freq. Thres.	.	.	.
	R^2	0.32	0.20	-0.12
Static Force	Act. Thres.	11N	8.6N	-2.4N
	Freq. Asymptote	60N	60N	0.0N
	Mean Rate	3.3	3.9	0.6
	Slope	-1.30	-0.53	-0.77
	Freq. Thres.	5.0N	6.0N	1.0N
	R^2	0.77	0.60	-0.17

TABLE G-27
EFFECT OF SALINE
REACTIVITY IN THE HORIZONTAL PLANE
UNIT #8

Test Condition		Pre	Post	Post-Pre
Dynamic Force	Act. Thres.	7.0N	5.0N	-2.0N
	Freq. Asymptote	48N	56N	8.0N
	Mean Rate	3.3	3.2	-0.1
	Slope	-0.78	-0.86	0.08
	Freq. Thres.	.	.	.
	R^2	0.37	0.73	0.36

LIST OF REFERENCES

Abe K and Kawamura Y (1973). A study on inhibition of masseteric a-motor fibre discharges by mechanical stimulation of the temporomandibular joint in the cat. Arch Oral Biol 18: 301-304.

Agerberg G (1988). Bite force after temporomandibular joint surgery. Int J Oral Maxillofac Surg 17: 177-180.

Albright D and Zimny ML (1987). Mechanoreceptors in the human medial meniscus. Anat Rec (Abstract) 218: 6A-7A.

Andres KH, von Düring M, Janig W and Schmidt RF (1980). Sensory innervation of the Achilles tendon by group III and IV afferent fibers. Anat Embryol 172:145-156.

Appenteng K, Lund JP and Sequin JJ (1982). Behavior of cutaneous mechanoreceptors recorded in mandibular division of gasserian ganglion of the rabbit during movements of lower jaw. J Neurophysiol 47: 151-166.

Awad EA (1973). Interstitial myofibrositis: Hypothesis of the mechanism. Arch Phys Med Rehabil 54: 449-453.

Baumann JA (1951). Contribution á l'etude de l'innervation de l'articulation temporomaxillaire. Compt rend Assoc Anat 38: 120.

Beaudeau DE and Jerge CR (1968). Somatotopic representation into the gasserian ganglion of tactile peripheral fields in the cat. Arch Oral Biol 131: 247-256.

Beck PW, Handwerker HO and Zimmerman M (1974). Nervous outflow from the cat's foot during noxious radiant heat stimulation. Brain Res 67: 373-386.

Bell WE (1969). Nonsurgical management of pain-dysfunction syndrome. J Am Dent Assoc 79: 161-170.

Berberich P, Hoheisel V and Mense S (1988). Effects of a carragenan-induced myositis on the discharge properties of group III and IV muscle receptors in the cat. J Neurophysiol 59: 1395-1409.

Bernick S (1962). The vascular and nerve supply to the temporomandibular joint of the rat. Oral Surg Oral Med Oral Path 15: 488-498.

Bifano CA, Grellner T, Houston G, Farr SC, Ehler WJ, Cissik JH and Chastain M (1990). Cryogenically preserved adult and juvenile goat mandibular condylar transplantation. Oral Surg Oral Med Oral Pathol 69: 291-298.

Birrell GJ, McQueen DS, Iggo A, and Grubb BD (1990). The effects of 5-HT on articular sensory receptors in normal and arthritic rats. Br J Pharmacol 101: 715-721.

Birrell GJ, McQueen DS, Iggo A and Grubb BD (1991). PGI_2-induced activation and sensitization of articular mechanoreceptors. Neuroscience Letters, 124: 5-8.

Boyd IA (1954). The histological structure of the receptors in the knee joint of the cat correlated with their physiological response. J Physiol (Lond) 124: 476-488.

Boyd IA and Roberts TDM (1953). Proprioceptive discharges from stretch-receptors in the knee joint of the cat. J Physiol (Lond) 122: 38-58.

Broekhuijsen ML and van Willigen JD. (1983). Factors influencing jaw position sense in man. Arch Oral Biol 28: 387-391.

Broton JG and Sessle BJ (1988). Reflex excitation of masticatory muscles induced by algesic chemicals applied to the temporomandibular joint of the cat. Arch Oral Biol 33: 741-747.

Broton JG, Hu JW and Sessle BJ (1988). Effects of temporomandibular joint stimulation on nociceptive and nonnociceptive neurons of the cat's trigeminal subnucleus caudalis (Medullary dorsal horn). J Neurophysiol 59: 1575-1589.

Burgess PR and Clark FJ (1969). Characteristics of knee joint receptors in the cat. J Physiol (Lond) 203: 317-335.

Burgess PR and Perl EF (1967). Myelinated afferent fibers responding specifically to noxious stimulation of the skin. J Physiol (Lond) 190: 541-562.

Burgess PR, Wei JY, Clark FJ and Simon J (1982). Signaling of kinesthetic information by peripheral sensory receptors. Ann Rev Neurosci 5: 171-187.

Burke D, Gandevia SC and Macefield G (1988). Responses to passive movement of receptors in joint, skin and muscle of the human head. J Physiol 402: 347-361.

Caffese RG, Carraro JJ and Albano EA (1973). Influence of temporomandibular joint receptors on tactile occlusal perception. J Periodont Res 8: 400-403.

Campbell JN, Meyer RA and LaMotte RH (1979). Sensitization of myelinated nociceptive afferents that innervate monkey hand. J Neurophysiol 42: 1669-1679.

Capra HF (1987). Localization and central projections of primary afferent neurons that innervate the temporomandibular joint in cats. Somatosensory Research 4: 201-213.

Capra NF and Gatipon GB (1981). Unit activity of trigeminal ganglion neurons recorded during jaw opening and closing. Society of Neuroscience Abstracts 6: 674.

Carlsson GE and Helkimo M (1972). Funktionell undersökning av tuggapparaten. In: Holst Nordish klinisk odontologi 8-1-1-21, Forlaget for Faglitteratur, Copenhagen.

Chen TT and Turner DF (1987). Sensory innervation of the temporomandibular joint. J Dent Res Abstracts 66: 1044.

Christensen LV and Troest T (1975). Clinical kinesthetic experiments on the lateral pterygoid muscle and temporomandibular joint in man. Scand J Dent Res 83: 238-244.

Christiansen EG (1922). Nogen undersökelser angaaende det naturlige of det kunstige tandsaets tuggeevhe. Norske Tandlaegeforen Tid 32: 259-288.

Clark FJ (1975). Information signalled by sensory fibers in medial articular nerve. J Neurophysiol 38: 1461-1472.

Clark FJ and Burgess PR (1975). Slowly adapting receptors in cat knee joint: Can they signal joint angle? J Neurophysiol 38: 1448-1463.

Clark FJ, Horch KW, Bach SM and Larson GF (1979). Contributions of cutaneous and joint receptors to static knee-position in man. J Neurophysiol 42: 877-88.

Clark GT, Carter MC and Beemsterboer PL (1984). Bite force to EMG ratio during various isometric tasks sustained to pain tolerance. Pain (Supplement) 2: 423.

Coggeshall RE, Hong KAP, Langford LA, Schaible H-G and Schmidt RF (1983). Discharge characteristics of fine medial articular afferents at rest and during passive movements of inflamed knee joints. Brain Res 272: 185-188.

Cohen LA (1955). Activity of knee joint proprioceptors recorded from the posterior articular nerve. Yale J Biol Med 28: 225-232.

Cooper B, Ahlquist M, Friedman RM and LaBanc J (1991). Properties of high threshold mechanoreceptors in goat oral mucosa. II. Dynamic and static reactivity in carrageenan-inflamed mucosa. J Neurophysiol 66: 1280-1290.

Cooper B, Ahlquist M, Friedman R, Loughner B and Heft M (1990). Mechanical sensitization of HTMS and its relation to tissue compliance. Society of Neuroscience Abstracts 16: 720.

Cooper B, Ahlquist M, Friedman R, Loughner B and Heft M (1991). Properties of high threshold mechanoreceptors in the oral mucosa. I: Responds to dynamic and static pressure. J Neurophysiol 66: 1272-1279.

Corbin B (1940). Observations in the peripheral distribution of fibers arising in the mesencephalic nucleus of the fifth cranial nerve. J Comp Neurol 73: 153-177.

Costen JB (1934). Syndrome of ear and sinus symptoms dependent upon disturbed function of the temporomandibular joint. Ann Otol Rhin Laryng 43: 1-15.

Craig AD and Burton H (1981). Spinal and medullary lamina 1 projection to nucleus submedius and medial thalamus: a possible pain center. J Neurophysiol 45: 443-466.

Dahlberg B (1942). The masticatory effect. Acta Med Scand (Supplement) 139: 1-156.

Darian-Smith I, Mutton P and Proctor R (1965). Functional organization of tactile cutaneous afferents within the semilunar ganglion and trigeminal spiral tract of the cat. J Neurophysiol 28: 682-694.

Davis DV (1945). Anatomy and physiology of diarthrodial joints. Ann Rheumat Dis 5: 29.

Deboever JA (1973). Functional disturbances of the temporomandibular joints. Oral Sci Rev 1: 100-117.

Dorn T, Schaible H-G and Schmidt RF (1991). Response properties of thick myelinated group II afferents in the medial articular nerve of normal and inflamed knee joints of the cat. Som and Mot Res 8: 127-136.

Dostrovsky JO and Broton JG (1985). Antidromic activation of neurons in the medullary dorsal horn from stimulation in nucleus submedius. Society of Neuroscience Abstracts 11: 411.

Dostrovsky JO and Guilbaud G (1990). Nociceptive responses in medial thalamus of the normal and arthritic rat. Pain 40: 93-104.

Dubner R, Sessle BJ and Storey AT (1978). The Neural Basis of Oral and Facial Function. Plenum, New York, p. 147-174.

Fields HL (1987). Pain. McGraw-Hill, New York, p. 79-99.

Fitzgerald M and Lynn D (1977). The sensitization of high threshold mechanoreceptors with myelinatde axons by repeated heating. J Physiol (Lond) 265: 549-563.

Foley JO (1960). A quantitative study of the functional components of the facial nerve. Am J Anat 107: 237-244.

Franks AS (1965). De beheersing van de bewegingen in het koakgewricht. Nederl T Tandheelk 72: 605.

Freeman MAR and Wyke B (1967). The innervation of the knee joint: An anatomical and histological study in the cat. J Anat 101: 505-532.

Friedman R, Cooper BY, Ahlquist ML and Loughner BA (1988). Sensitization of high threshold mechanoreceptors in the oral cavity of the goat. Society of Neuroscience Abstracts 14: 562.

Frommer J and Monroe CW (1966). The morphology and distribution of nerve fibers and endings associated with the mandibular joint of the mouse. J Dent Res 45: 1762-1766.

Frost HM (1968). Musculoskeletal pain. In: Facial Pain. CC Alling (ed), Lea and Febiger, Philadelphia, p. 153-173.

Garcia-Leme, J (1989). Hormones and Inflammation. CRC Press Inc, Boca Raton, Florida, p. 61-64.

Gautron M and Guilbaud G (1982). Somatic responses of ventrobasal thalamic neurons in polyarthritic rats. Brain Res 237: 459-471.

Greenfield BE and Wyke B (1966). Reflex innervation of the temporomandibular joint. Nature (Lond) 211: 940-941.

Griffin CJ and Harris R (1975). Innervation of the temporomandibular joint. Aust Dent J 20: 78-85.

Griffin CJ and Malor R (1974). An analysis of controlled mandibular movement. Monogr Oral Sci Physiol, Karger, Basel, Vol 4, p. 151-169.

Griffin CJ, Sharpe CJ and Gee E (1965). Inhibition of the linguo-mandibular reflex. I. Golgi type organs at the pes menisci. Aust Dent J 10: 376-379.

Grigg P (1975). Mechanical factors influencing response of joint afferent neurons from cat knee. J Neurophysiol 38: 1473-1484.

Grigg P, Finerman GA and Riley LH (1973). Joint-position sense after total hip replacement. J Bone Joint Surg 55A: 1016-25.

Grigg P and Greenspan BJ (1977). Response of primate joint afferent neurons to mechanical stimulation of knee joint. J Neurophysiol 40: 1-8.

Grigg P and Hoffman AH (1989). Calibrating joint capsule mechanoreceptors as in vivo soft tissue load cells. J Biomechanic 22: 781-785.

Grigg P, Hoffman AH and Fogarty KE (1982a). Properties of Golgi-Mazzoni afferents in cat knee joint capsule, as revealed by mechanical studies of isolated joint capsule. J Neurophysiol 47: 31-40.

Grigg P, Hoffman AH and Fogarty KE (1982b). Properties of Ruffini afferents revaled by stress analysis of isolated sections of cat knee capsule. J Neurophysiol 47: 41-57.

Grigg P, Schaible H-G and Schmidt RF (1986). Mechanical sensitivity of Group III and IV afferents from posterior articular nerve in normal and inflamed cat knee. J Neurophysiol 55: 635-643.

Grubb BD, Birrell GJ, McQueen DS and Iggo, A (1991). The role of PGE in the sensitization of mechanoreceptors in normal and inflamed ankle joints of the rat. Exp Brain Res 84: 383-392.

Grubb BD, McQueen DS, Iggo A, Birrell GJ and Dutia MB (1988). A study of 5-HT-receptors associated with afferent nerves located in normal and inflamed rat ankle jonts. Agents and Actions 25: 216-218.

Guerrier Y and Bolonyi F (1948). L'innervation de l'articulation temporo-maxillaire. Ann d'oto-laryng 65: 109.

Guilbaud G (1988). Peripheral and central electrophysiological mechanisms of joint and muscle pain. In: Proceedings of the Vth World Congress on Pain. R Dubner, GF Gebhart and MR Bond (eds), Elsevier, New York, p. 201-215.

Guilbaud G, Iggo A and Tegner R (1985). Sensory receptors in ankle joint capsules of normal and arthritic rats. Exp Brain Res 58: 29-40.

Guilbaud G, Peschanski M, Gautron M and Binder D (1980). Neurons responding to noxious stimulation in VB complex and caudal adjacent regions in the thalamus of the rat. Pain 8: 303-318.

Hagen-Torn O (1882). Entivicklung und Bau der Synovialmembranen. Arch mikrosk Anat 21: 591.

Hall MB, Parker T, Cherry J and Ballinger WE (1985). Innervation of the bilaminar zone in human temporomandibular joints. In: Case Reports and Outline, 67th Annual Meeting and Scientific Sessions. AAOMS, Washington DC, p. 77.

Handwerker HO, Anton and Rech PW (1987). Discharge patterns of afferent cutaneous nerve fibers from the rat's tail during prolonged noxious mechanical stimulation. Exp. Brain Res 66: 421-431.

Handwerker HO, Kilo S and Rech PW (1991). Unresponsive afferent nerve fibers in the sural nerve of the rat. J Physiol 435: 229-242.

He X, Schepelmann K, Schaible H-G and Schmidt RF (1990). Capsaicin inhibits reponses of fine afferents from the knee joint of the cat to mechanical and chemical stimuli. Brain Research, 530: 147-150.

Helkimo E, Carlson GE and Carmeli Y (1975). Bite force in patients with functional disturbances of the masticatory system. J Oral Rehab 2: 397-406.

Helkimo M (1974). Studies of function and dysfunction of the masticatory system. II. Index for anammestic and clinical dysfunctiona and occlusal state. Sved Dent J 67: 101-121.

Helkimo M (1979). Epidemiological surveys of dysfunction of the masticatory system. In: Temporomandibular Joint Function and Dysfunction. GA Zarb and C Carlsson (eds) Mosby, St. Louis, p. 175.

Henry ML, Johnson L, Mahan PE and Westrum L (1986). Somatotopic organization of dental structures within the feline V ganglion. J Dent Res (Suppl) 64: 210.

Heppelman B, Herbert MK, Schaible H-G and Schmidt RG (1987). Morphological and physiological characteristics of the innervation of cat's normal and arthritic knee joint. In: Effects of Injury on Trigeminal and Spinal Somatosensory Systems. LM Pubols and BJ Sessle (eds). Alan Liss Inc, New York, p. 19-27.

Heppleman B, Schaible H-G and Schmidt RF (1985). Effects of prostaglandins E_1 and E_2 on the mechanosensitivity of group III afferents from normal and inflamed cat knee joints. In: Advances in Pain Research and Therapy. HF Fields, R Dubner and F Cervero (eds), Raven Press, New York, p. 91-101.

Hilton J (1879). In: Jacobson WHA. Rest and pain. Butterworth and Company, New York, p. 96.

Hoffman AH and Grigg P (1989). Measurement of joint capsule tissue loading in the cat knee using calibrated mechanoreceptors. J Biomechanics 22: 787-791.

Hromada J (1960). Beitrag zur Kenutnis der Entwicklung und der Variabilitat der Lamellenkörperchen in der Gelenkkapsel und im periartikulären Gewebe beim meschlichen Fetus. Acta Anat 40: 27-40.

Ishibashi K (1966). Studies in innervation of human mandibular joint. Jap J Oral Biol 8: 46-57.

Ishibashi K (1974). Innervation of human temporomandibular joint in adult. Bull Tokyo Med Dent Univ 21 (Suppl): 86-88.

Jerge CR (1964). The neurologic mechanism underlying cyclic jaw movements. J Prosth Dent 14: 667-681.

Kanaka R, Schaible H-G and Schmidt RF (1985). Activation of fine articular afferent units by bradykinin. Brain Res 327: 81-90.

Kawamura Y (1980). Neurophysiology. In: The Temporomandibular Joint. A Biological Basis for Clinical Practice. BG Sarnat and DM Laskin (eds), Charles Thomas, Springfield, Illinois, p. 114-126.

Kawamura Y and Abe K (1974). Role of sensory information from temporomandibular joint. Bull Tokyo Med Dent Univ 21 (Suppl) 78-82.

Kawamura Y and Majima T (1964). Temporomandibular joint's sensory mechanisms controlling activities of jaw muscles. J Dent Res 43: 150.

Kawamura Y, Majima T and Kato I (1967). Physiological role of deep mechanoreceptors in temporomandibular joint capsule. J Osaka Univ Dent Sch 7: 63-76.

Kayser V and Guilbaud G (1984). Further evidence for changes in the responsiveness of somatosensory neurons in arthritic rats: a study in the posterior intralaminar region of the thalmus. Brain Res 323: 144-147.

Keller JH and Moffet BC (1968). Nerve endings in the temporomandibular joint of the rhesus macaque. Anat Rec 160: 587-594.

Kerr FWL (1962). Correlated light and electron microscopic observations on the normal trigeminal gangion and sensory root in man. J Neurosurg (Suppl) 26: 132-137.

Kerr FWL and Lysak WR (1964). Somatotopic organization of trigeminal ganglion neurons. Arch Neurol 11: 593-602.

Kitamura H (1974). Development of the Temporomandibular Joint Innervation. Bull Tokyo Med Dent Univ 21 (Suppl): 83-85.

Klineberg I (1971). Structure and function of temporomandibular joint innervation. Am Roy Coll Surg 49: 268-288.

Klineberg I (1980). Influence of temporomandibular articular mechanoreceptors on functional jaw movements. J Oral Rehab 7: 307-317.

Klineberg I, Greenfield BE and Wyke BD (1970). Afferent discharges from temporomandibular articular mechanoreceptors. Arch Oral Biol 15: 935-952.

Klineberg I, Greenfield BE and Wyke BD (1971). Afferent from discharges from temporomandibular articular mechanoreceptors: an experimental analysis of their behavorial characteristics in the cat. Arch Oral Biol 16: 1463-1479.

Kojima Y (1990). Convergence patterns of afferent information from the temporomandibular joint and masseter muscle in the trigeminal subnucleus caudalis. Brain Research Bulletin 24: 609-616.

Kreutziger KL and Mahan PE (1975). Temporomandibular degenerative joint disease. Part I. Anatomy, pathophysiology and clinical description. Oral Surg Oral Med Oral Pathol 40: 165-182.

Lamour Y, Guilbaud G and Willer JC (1983). Altered properties and laminar distribution of neuronal responses to peripheral stimulation in the Sm I cortex of the arthritic rat. Brain Res 273: 183-187.

Larsson LE and Thilander B (1964). Mandibular positioning. The effect of pressure on the joint capsule. Acta Neurol Scand 40: 131-143.

Lemke R, Dolwick MF, Hogan B and Rugh JO (1987). Masticatory efficiency of post-TMJ surgery patients. IADR Abstracts 66:118.

Li JCR (1969). Statistical Inference. Edwards Brothers, Ann Arbor, Michigan.

Limwongee V (1986). Cell body location of trigeminal sensory neuron innervating the temporomandibular joint in rat, cat and monkey. Society of Neuroscience Abtracts 12: 333.

Loos S (1963). A simple test of masticatory function. Int Dent J 13: 615-616.

Loughner B, Larkin LH and Mahan PE (1990). Nerve entrapment in the lateral pterygoid muscle. Oral Surg Oral Med Oral Path 69: 299-306.

Lund JP and Matthews B (1981). Responses of temporomandibular joint afferents recorded in the gasserion ganglion of the rabbit to passive movements of the mandible. In: Oral-Facial Sensory and Motor Functions. Y Kawamura and R Dubner (eds), Quintessence, Chicago, p. 153-160.

Macefield G, Gandevia SC and Burke D (1990). Perceptual responses to microstimulation of single afferents innervating joints, muscles and skin of the human hand. J Physiol 429: 113-129.

Mahan PE and Alling CC (1991). Facial Pain. 3rd edition Lea and Febiger, Philadelphia.

Manly RS and Braley LC (1950). Masticatory Performance and Efficiency. J Dent Res 29: 448-462.

Marfurt CF (1981). The somatotopic organization of the cat trigeminal ganglia as determined by the horseradish peroxidase technique. Anat Rec 201: 105-118.

McCall WD, Farias MC, Williams WJ and Bement SL (1974). Static and dynamic responses of slowly adapting joint receptors. Brain Res 70: 221-243.

McQueen DS, Iggo A, Birrell GJ and Grubb BD (1991). Effects of paracentamol and aspirin on neural activity of joint mechanoreceptors in adjuvant arthritis. Br J Pharmacol 104: 178-182.

Mense S and Schmidt RF (1974). Activation of group IV afferent units from muscle by algesic agents. Brain Res 72: 305-310.

Morimoto T and Kawamura Y. (1978). Interdental thickness discrimination and position sense of the mandible. In: Oral Physiology and Occlusion. JH Perryman (ed), Pergaman, New York, p. 149-169.

Neugebauer V and Schaible H-G (1990). Evidence for a central component in the sensitization of spinal neurons with joint input during development of acute arthritis in cat's knee. J Neurophysiol 64: 299-311.

Okeson JP (1989). Management of temporomandibular disorders and occlusion. 2nd edition,Mosby, St Louis, p. 87-104.

Olson A (1969). Temporomandibular joint function and functional disturbances. Dent Clinics North Am 13: 643-648.

Polacek P (1966). Receptors of the joints: Their structure, variability and classification. Acta Facultat Med Universitat Brunensis 23: 1-107.

Posselt U and Thilander B (1965). Influence of the innervation of the temporo-mandibular capsule on mandibular border movements. Acta Odont Scand 23: 601-613.

Posselt V (1968). Physiology of occlusion and rehabilitation. 2nd edition, Blackwell, Oxford.

Ransjo K and Thilander B. (1963). Perception of mandibular position in cases of temporomandibular joint disorders. Odontolgiska Foreningens Tidskrift 71: 134-144.

Reeh PW, Bayer L, Kocher L and Handwerker HO (1987). Sensitization of nociceptive cutaneous nerve fibers from the rat's tail by noxious mechanical stimulation. Exp Brain Res 65: 505-512.

Rocabado M (1983). Arthrokinematics of the temporomandibular joint. Dent Clin North Am 27: 573-594.

Rominger JW and Rugh JD (1986). Comparison of masticatory performance of TMJ dysfunction subjects and controls. J Dent Res 29: 448-462.

Romfh JH, Capra NF and Gatipon GB (1979). The trigeminal nerve and the temporomandibular joint of the cat: a horseradish peroxidase study. Exp Neurol 65: 99-106.

Rose JE and Mountcastle VB (1959). Touch and kinesthesia. In: Handbook of Physiology. J Field (ed), Amer Physiol Soc, Wash DC, vol 1, p. 387-429.

Rossi A and Grigg P (1982). Characteristics of hip joint mechanoreceptors in the cat. J Neurophysiol 27: 573-594.

Rossie F (1950). Sur l'innervation fine de la capsule articularie. Acta Anat 10: 161-232.

Rüdinger N (1857). Die Gelenknerven des menschlichen. Körpers, Erlangen.

Samuel EP (1952). The autonomic and somatic innervation of the articular capsule. Anat Rec 113: 53-70.

Schaible HG (1983). Sensitization by prostaglandin E_1. Naunyn-Schmiedebergs Arch Pharmacol (Suppl) 352: R98.

Schaible HG and Schmidt RF (1983a). Activation of groups III and IV sensory units in medial articular nerve by local mechanical stimulation of knee joint. J Neurophysiol 49: 35-44.

Schaible HG and Schmidt RF (1983b). Responses of fine medial articular nerve afferents to passive movement of knee joint. J Neurophysiol 49: 1118-1126.

Schaible HG and Schmidt RF (1984). Mechanosensibility of joint receptors with fine afferent fibers. Exp Brain Res (Suppl 9), p. 284-297.

Schaible HG and Schmidt RF (1985). Effects of an experimental arthritis in the sensory properties of fine articular afferent units. J Neurophys 54: 1109-1122.

Schaible HG, Schmidt RF and Willis WD (1986). Responses of spinal cord neurons to stimulation of articular afferent fibers in the cat. J Physiol 372: 575-593.

Schaible HG and Schmidt RF (1988a). Excitation and sensitization of fine articular afferents from cat's knee joint by prostaglandin E_2. J Physiol 403: 91-104.

Schaible HG and Schmidt RF (1988b). Direct observations of the sensitization of articular afferents during an experimental arthritis. In: Proceedings of the Vth World Congress of Pain. R Dubner, GF Gebhart, MR Bond (eds), Elsevier, New York, p. 44-50.

Schellhas KP, Wilkes CH and Baker CC (1989). Facial pain, headache and temporomandibular joint inflammation. Headache 29: 228-231.

Schmid F (1969). On the nerve distribution of the temporomandibular joint capsule. Oral Surg Oral Med Oral Path 28: 63-65.

Sessle BJ and Greenwood IF (1976). Inputs to trigeminal brainstem neurons from facial, oral, tooth, and pharyngolaryngeal tissues. I. Responses to innocuous and noxious stimuli. Brain Res 117: 211-226.

Sicher H (1955). Structural and functional basis for disorders of the temporomandibular articulation. J Oral Surg 13: 275-279.

Sicher H (1960). Oral anatomy. 3rd edition, Mosby, St. Louis, p. 166-168.

Siirila HA and Laine P (1972). Sensory thresholds in discriminating differences in thickness between the teeth by different degrees of mouth opening. Proc Finn Dent Soc 68: 134-139.

Sheikoleham A, Möller E and Lous I (1982). Postural and maximal activity in elevators of mandible before and after treatment of functional disorders. Scand J Dent Res 90: 37-46.

Sherrington CS (1947). The Integrative Action of the Nervous System. Yale Univesity Press, New Haven, Connecticut p. 228.

Skoglund S (1956). Anatomical and physiological studies of knee joint innervation in the cat. Acta Physiol Scand (Supplement 36) 124: 1-101.

Skoglund S. (1973). Joint receptors and kinaesthesis. In: Handbook of Sensory Physiology. A Iggo (ed), Vol II, Somatosensory System. Springer-Verlag, Berlin, p. 111-136.

Solberg, WK (1987). Epidemiological findings of importance to management of temporomandibular disorders. In: Perspectives in Temporomandibular Disorders. GT Clark and WK Solbert (eds). Quintessence Publishing Co, Chicago, p. 27-44.

Thilander B (1961). Innervation of temporomandibular joint capsule in man. Trans R School Dent Umea 2: 1-67.

Travell J (1976). Myofascial trigger points: clinical view. In: Advances in Pain Research and Therapy. JJ Bonica and D Albe-Fessard (eds), Raven, New York, p. 919-926.

Turnbull WD (1970). Mammalian masticatory apparatus. Fieldiana. Geology. Vol 18, No 2 (Field Museum of Natural History, Chicago).

van den Berghe L, de Boever JA, Brockhuijsen ML and van Willigen JD (1987). On the perception of the preferred jaw position in patients with symptoms of temporomandibular disorders. J Craniomand Pract 5: 344-350.

van Willigen JD, Broekhuijsen ML, de Bont LGM and van der Kuijl B (1986). On the perception of jaw position and bite force by subjects with craniomandibular disorders. J Craniomand Pract 4: 128-133.

Vinegar R, Truax JF, Selph JH, Johnston PR, Venable AL and McKenzie KK (1987). Pathway to carrageenan-induced inflammation in the hind limb of the rat. Federation Proc 46: 118-126.

Weinmann JP and Sicher H (1951). Histophysiology of the temporomandibular jont. In: The Temporomandibular Joint. BG Sarnat (ed), Thomas, Springfield, p. 71-75.

Widenfalk B and Wiberg M (1990). Origin of sympathetic and sensory innervation of the temporo-mandibular joint. A retrograde axonal tracing study in the rat. Neuroscience Letters 109: 30-35.

Williams WN, Henry MA and Mahan PE (1989). The effect of experimental anesthetization of temporomandibular joint superior cavity on bite force discrimination. J Craniomand Pract 7: 194-199.

Williams WN, LaPointe LL, Mahan PE and Cornell CE (1984). The influence of TMJ and central incisors impairment on bite force discrimination. J Craniomand Pract 2: 119-124.

Willis WD and Coggeshall RE (1978). Sensory Mechanisms of the Spinal Cord. Chapter 2. Plenum Press, New York, p. 9-51.

Yemm R (1979). Neurophysiologic studies of temporomandibular joint dysfunction. In: Temporomandibular Joint Function and Dysfunction. GA Zarb and CE Carlsson (eds), Mosby, St Louis, p. 215-237.

Zarb GA and Carlsson GE (1988). Examination and differential diagnosis of occlusal problems. In: A Textbook of Occlusion. HD Mohl, GA Zarb, GE Carlsson and JO Rugh (eds), Quintessence, Chicago, p. 185-207.

Zeller J, Wussbarth E, Baruth B, Mielke H and Deicher H (1983). Serotonin content of platelets in inflammatory rheumatic diseases. Correlation with clinical activity. Arthritis Rheum 26: 532-540.

Zimny ML (1988). Mechanoreceptors in articular tissue. Am J Anat 182: 16-32.

Zimny ML and St. Onge M (1987). Mechanoreceptors in the temporomandibular articular disk. J Dent Res 66: 237.

Zucker E and Welker WI (1969). Coding of somata sensory input by vibrissae neurons in the rat's trigeminal ganglion. Brain Res 12: 138-156.

BIOGRAPHICAL SKETCH

I was born on December 13, 1943, in Greensburg, Pennsylvania. I attended Pennsylvania State University between 1961 and 1965 where I received a Bachelor of Science degree in biochemistry. I attended New York University between 1965 and 1969 where I received a Doctor of Dental Surgery degree in dentistry. In 1985 and 1986, I attended the University of Florida as a postgraduate fellow in the Facial Pain Center of the dental school. I received a Masters of Anatomy degree in the Department of Anatomy and Cell Biology, University of Florida between 1986 and 1987. I pursued a Doctor of Philosophy degree in the Department of Oral Biology, University of Florida, between 1987 and 1992, and will graduate in May, 1992.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Parker Mahan, Chairman
Distinguished Service Professor
of Oral Biology

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Brian Cooper, Cochairman
Assistant Professor of Neuroscience

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Charles Gibbs
Professor of Oral Biology

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Charles Vierck
Professor of Neuroscience

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Lynn Larkin
Professor of Anatomy
and Cell Biology

This dissertation was submitted to the Graduate Faculty of the College of Medicine and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

May 1992

Dean, College of Medicine

Dean, Graduate School